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**OMNIBUS SOLICITATION OF THE  
NATIONAL INSTITUTES OF HEALTH,  
CENTERS FOR DISEASE CONTROL AND PREVENTION,  
AND FOOD AND DRUG ADMINISTRATION FOR**

**SMALL BUSINESS  
INNOVATION RESEARCH  
(SBIR)**

**AND**

**SMALL BUSINESS  
TECHNOLOGY TRANSFER  
(STTR)**

**GRANT APPLICATIONS**

**GRANT APPLICATION RECEIPT DATES**

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**National Institutes of Health**  
April 1, August 1, December 1, 2001 (SBIR and STTR)

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**Centers for Disease Control and Prevention**  
August 1 and December 1, 2001 (SBIR)

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**Food and Drug Administration**  
April 1, August 1, December 1, 2001 (SBIR)

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# TABLE OF CONTENTS

<b>IMPORTANT INFORMATION AND REMINDERS IN THIS SOLICITATION .....</b>	<b>1</b>
<b>I. GENERAL PROGRAM DESCRIPTION .....</b>	<b>3</b>
A. SBIR/STTR PROGRAMS: THREE PHASES .....	3
B. FAST-TRACK APPLICATIONS .....	4
C. PURPOSE OF SOLICITATION .....	4
D. SBIR/STTR PROGRAM ELIGIBILITY .....	5
ORGANIZATIONAL CRITERIA .....	5
PERFORMANCE OF RESEARCH AND ANALYTICAL WORK BY THE APPLICANT ORGANIZATION .....	5
SBIR .....	5
STTR .....	6
PERFORMANCE SITE CRITERIA.....	6
PRINCIPAL INVESTIGATOR CRITERIA .....	6
SBIR .....	6
STTR .....	7
<b>II. AGENCY CONTACT FOR INFORMATION .....</b>	<b>8</b>
PROGRAM OFFICIALS/AGENCY CONTACT INFORMATION .....	8
<b>III. DEFINITIONS .....</b>	<b>10</b>
<b>IV. GRANT APPLICATION PREPARATION INSTRUCTIONS AND REQUIREMENTS.....</b>	<b>13</b>
A. LIMITATIONS ON LENGTH OF APPLICATION .....	13
B. TYPE SIZE .....	14
C. FORM PAGE ENTITLED "PERSONAL DATA ON PRINCIPAL INVESTIGATOR" .....	14
D. MARKET RESEARCH.....	14
E. PRIOR SBIR PHASE II AWARDS.....	15
F. ASSIGNMENT OF GRANT APPLICATIONS.....	15
<b>V. SUBMISSION OF SBIR/STTR GRANT APPLICATIONS.....</b>	<b>15</b>
A. RECEIPT DATES .....	15
RECEIPT OF SBIR/STTR PHASE II APPLICATIONS (NON-"FAST-TRACK") .....	16
B. NUMBER OF COPIES.....	16
C. BINDINGS AND PACKAGING .....	16
D. MAILING AND/OR DELIVERY ADDRESSES .....	16
E. NOTIFICATION OF RECEIPT .....	16
SAMPLE GRANT APPLICATION ASSIGNMENT NUMBER.....	17
F. INCOMPLETE APPLICATIONS.....	17
G. SUPPLEMENTARY OR CORRECTIVE INFORMATION .....	17
<b>VI. METHOD OF SELECTION AND EVALUATION CRITERIA.....</b>	<b>17</b>
A. REVIEW PROCESS.....	17
SCIENTIFIC REVIEW GROUPS .....	17
NATIONAL ADVISORY COUNCIL OR BOARD .....	18
B. RELEASE OF GRANT APPLICATION REVIEW INFORMATION .....	18
C. SBIR/STTR REVIEW CRITERIA .....	18
PHASE II APPLICATIONS .....	19
PHASE I/PHASE II FAST TRACK APPLICATIONS.....	19
D. FUNDING DECISIONS .....	19
E. REVISION AND RESUBMISSION OF GRANT APPLICATIONS .....	20
AMENDED (REVISED) APPLICATIONS.....	20
F. SUBMISSION OF SIMILAR GRANT APPLICATIONS BY THE APPLICANT ORGANIZATION.....	20
G. PHASE I/PHASE II FAST-TRACK REVIEW OPTION (APPLICABLE TO NIH ONLY) .....	20
SBIR/STTR FAST-TRACK APPLICATION INSTRUCTIONS AND REQUIREMENTS .....	21

<b>VII. CONSIDERATIONS</b>	<b>22</b>
A. AWARDS	22
B. REPORTS	22
FINAL FINANCIAL STATUS REPORT (FSR) (OMB 269)	22
FINAL PROGRESS REPORT	22
FINAL INVENTION STATEMENT AND CERTIFICATION	23
ANNUAL UTILIZATION REPORT	23
C. PAYMENT SCHEDULE	23
D. LIMITED RIGHTS INFORMATION AND DATA	23
PROPRIETARY INFORMATION	23
TITLE TO EQUIPMENT AND SUPPLIES	24
RIGHTS TO DATA DEVELOPED UNDER SBIR/STTR FUNDING AGREEMENT	24
COPYRIGHTS	24
INVENTIONS	24
PATENTS	25
RESEARCH TOOLS/UNIQUE RESEARCH RESOURCES	25
E. PROFIT OR FEE	25
F. JOINT VENTURES AND LIMITED PARTNERSHIPS	25
G. AMERICAN-MADE EQUIPMENT AND PRODUCTS	25
H. TERMS AND CONDITIONS OF AWARD	26
I. ADDITIONAL INFORMATION	26
<b>VIII. SCIENTIFIC AND TECHNICAL INFORMATION SOURCES</b>	<b>27</b>
<b>IX. MODEL AGREEMENT FOR ALLOCATION OF RIGHTS</b>	<b>27</b>
<b>X. GRANTS: PROGRAM DESCRIPTIONS AND RESEARCH TOPICS</b>	<b>28</b>
<b>OFFICE OF PUBLIC HEALTH AND SCIENCE, OFFICE OF RESEARCH INTEGRITY (ORI)</b>	<b>28</b>
<b>NATIONAL INSTITUTES OF HEALTH (NIH)</b>	<b>29</b>
NATIONAL INSTITUTE ON AGING (NIA)	30
BIOLOGY OF AGING	30
BEHAVIORAL AND SOCIAL RESEARCH	32
NEUROSCIENCE AND NEUROPSYCHOLOGY OF AGING	35
GERIATRICS	36
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE	37
NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)	38
PHARMACEUTICAL DEVELOPMENT FOR ALCOHOLISM TREATMENT	38
DIAGNOSTIC ASSESSMENT OF ALCOHOL USE DISORDERS AND COMORBIDITY	38
TREATMENT OF ALCOHOLISM	39
MEASUREMENT OF ALCOHOL CONSUMPTION/IMPAIRMENT	39
PREVENTION	40
TRAINING IN ALCOHOLISM ASSESSMENT AND TREATMENT TECHNIQUES	40
FETAL ALCOHOL SYNDROME (FAS) AND ALCOHOL-RELATED BIRTH DEFECTS	41
SCIENCE EDUCATION	41
RESEARCH TOOLS	42
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE	42
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)	42
DIVISION OF AIDS	42
DIVISION OF ALLERGY, IMMUNOLOGY, AND TRANSPLANTATION	44
DIVISION OF MICROBIOLOGY AND INFECTIOUS DISEASES	45
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE	47
NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)	47
ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES	48
MARKERS OF OSTEOARTHRITIS	49
MUSCLE BIOLOGY, EXERCISE PHYSIOLOGY AND SPORTS MEDICINE	50
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF THE INSTITUTE	51

NATIONAL CANCER INSTITUTE (NCI).....	51
DIVISION OF CANCER BIOLOGY .....	52
DIVISION OF CANCER CONTROL AND POPULATION SCIENCES .....	58
DIVISION OF CANCER TREATMENT AND DIAGNOSIS .....	59
DIVISION OF CANCER PREVENTION .....	67
OTHER RESEARCH TOPICS WITHIN THE MISSION OF INSTITUTE .....	69
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD) .....	70
POPULATION RESEARCH.....	70
RESEARCH FOR MOTHERS AND CHILDREN.....	72
MEDICAL REHABILITATION RESEARCH .....	73
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	73
NATIONAL INSTITUTE ON DRUG ABUSE (NIDA).....	73
DIVISION OF TREATMENT RESEARCH AND DEVELOPMENT.....	73
DIVISION OF BASIC NEUROSCIENCE AND BEHAVIORAL RESEARCH (DNBR).....	80
OFFICE OF SCIENCE POLICY AND COMMUNICATIONS (OSPC) .....	85
DIVISION OF EPIDEMIOLOGY, SERVICES AND PREVENTION RESEARCH (DESPR) .....	85
CENTER ON AIDS AND OTHER MEDICAL CONSEQUENCES OF DRUG ABUSE (CAMCODA).....	90
OTHER RESEARCH TOPICS WITHIN THE MISSION OF THE INSTITUTE.....	91
NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD) .....	92
HEARING PROGRAM .....	92
BALANCE/VESTIBULAR PROGRAM .....	92
VOICE, SPEECH, AND LANGUAGE PROGRAMS.....	92
SMELL AND TASTE PROGRAM .....	93
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	93
NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR) .....	93
INHERITED DISEASES AND DISORDERS .....	93
INFECTIOUS DISEASES.....	94
NEOPLASTIC DISEASES .....	95
CHRONIC DISABLING DISEASES .....	95
BIOMATERIALS, BIOMIMETICS, AND TISSUE ENGINEERING .....	96
BEHAVIOR, HEALTH PROMOTION AND ENVIRONMENT .....	97
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	97
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK) .....	98
DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES .....	98
DIGESTIVE DISEASES AND NUTRITION .....	101
KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES .....	102
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	105
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS) .....	105
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	106
NATIONAL EYE INSTITUTE (NEI) .....	107
RETINAL DISEASES PROGRAM .....	107
CORNEAL DISEASES PROGRAM.....	107
LENS AND CATARACT PROGRAM .....	107
GLAUCOMA PROGRAM.....	107
STRABISMUS, AMBLYOPIA, AND VISUAL PROCESSING PROGRAM .....	107
VISUAL IMPAIRMENT AND ITS REHABILITATION PROGRAM .....	107
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	107
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS) .....	108
DIVISION OF CELL BIOLOGY AND BIOPHYSICS .....	108
DIVISION OF GENETICS AND DEVELOPMENTAL BIOLOGY .....	109
DIVISION OF PHARMACOLOGY, PHYSIOLOGY, AND BIOLOGICAL CHEMISTRY .....	109
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	111
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI).....	111
HEART AND VASCULAR DISEASES .....	112
LUNG DISEASES.....	113
BLOOD DISEASES AND RESOURCES .....	115
EPIDEMIOLOGY AND CLINICAL APPLICATIONS.....	116
OTHER RESEARCH TOPIC(S) WITHIN THE MISSION OF INSTITUTE.....	117
NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) .....	118

DNA SEQUENCING.....	118
HUMAN GENOME SEQUENCE VARIATION .....	118
COMPARATIVE GENOMICS .....	118
FUNCTIONAL GENOMICS .....	119
BIOINFORMATICS AND COMPUTATIONAL BIOLOGY .....	119
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	119
NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) .....	119
DIVISION OF NEUROSCIENCE AND BASIC BEHAVIORAL SCIENCE.....	119
DIVISION OF MENTAL DISORDERS, BEHAVIOR AND AIDS.....	127
NIMH CENTER FOR MENTAL HEALTH RESEARCH ON AIDS.....	130
DIVISION OF SERVICES AND INTERVENTION RESEARCH .....	131
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	136
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS) .....	136
NEURODEVELOPMENT .....	136
NEUROGENETICS .....	137
REPAIR AND PLASTICITY .....	137
SYSTEMS AND COGNITIVE NEUROSCIENCE/CHANNELS, SYNAPSES AND CIRCUITS.....	139
NEURODEGENERATION .....	139
NEURAL ENVIRONMENT .....	139
TECHNOLOGY DEVELOPMENT .....	140
OTHER RESEARCH TOPICS WITHIN MISSIONS OF INSTITUTE .....	141
NATIONAL INSTITUTE OF NURSING RESEARCH (NINR).....	141
RESEARCH AND DEVELOPMENT OF TECHNOLOGIES THAT PROMOTE ALLEVIATION, ADAPTATION, OR MANAGEMENT OF SYMPTOMS.....	142
RESEARCH AND DEVELOPMENT OF TECHNOLOGIES TO ENHANCE SELF CARE AND CLINICAL CARE .....	142
OTHER RESEARCH TOPIC(S) WITHIN THE MISSION OF INSTITUTE.....	142
NATIONAL CENTER FOR RESEARCH RESOURCES (NCRR).....	142
RESEARCH AND DEVELOPMENT IN INSTRUMENTATION AND SPECIALIZED TECHNOLOGIES FOR BIOMEDICAL RESEARCH .....	142
RESEARCH AND DEVELOPMENT IN COMPARATIVE MEDICINE.....	143
CLINICAL TECHNOLOGY APPLICATIONS.....	144
DEVELOPMENT OF DISCOVERY-ORIENTED SOFTWARE FOR SCIENCE EDUCATION.....	144
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF CENTER .....	144
NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM) .....	145
EDUCATION AND PUBLIC INFORMATION.....	145
PATIENT MANAGEMENT .....	145
BOTANICAL PRODUCTS.....	145
RESEARCH-RELATED ISSUES.....	145
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF THE CENTER .....	146
NATIONAL LIBRARY OF MEDICINE (NLM) .....	146
MOLECULAR BIOLOGY .....	146
MEDICAL INFORMATICS.....	146
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF NLM.....	147
TRANS-NIH RESEARCH PROGRAMS .....	147
DEVELOPMENT OF SYNTHETIC AND NATURAL BIOMATERIAL REFERENCE MATERIALS.....	147
NATIONAL CENTER ON SLEEP DISORDERS RESEARCH .....	148
<b>CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC).....</b>	<b>149</b>
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH).....	149
CONTROL TECHNOLOGY AND PERSONAL PROTECTIVE EQUIPMENT.....	149
EXPOSURE ASSESSMENT METHODS.....	150
INTERVENTION EFFECTIVENESS RESEARCH.....	150
SURVEILLANCE RESEARCH METHODS .....	151
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF INSTITUTE .....	151
NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC) .....	152
PREVENTION .....	152
ACUTE CARE .....	153
REHABILITATION.....	153

OTHER RESEARCH TOPIC(S) WITHIN MISSION OF CENTER .....	154
NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP) .....	154
ARTHRITIS AND OTHER RHEUMATIC CONDITIONS .....	154
OFFICE ON SMOKING AND HEALTH .....	155
NATIONAL IMMUNIZATION PROGRAM (NIP) .....	156
OTHER RESEARCH TOPIC(S) WITHIN THE MISSION OF THE PROGRAM .....	156
NATIONAL CENTER FOR HIV, STD, AND TB PREVENTION (NCHSTP) .....	156
NATIONAL CENTER FOR ENVIRONMENTAL HEALTH (NCEH) .....	157
ENVIRONMENTAL HAZARDS AND HEALTH EFFECTS .....	157
EMERGENCY AND ENVIRONMENTAL HEALTH SERVICES .....	157
ENVIRONMENTAL HEALTH LABORATORY SCIENCES .....	158
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF CENTER .....	160
<b>FOOD AND DRUG ADMINISTRATION (FDA) .....</b>	<b>161</b>
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER) .....	161
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER) .....	161
CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN) .....	162
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH) .....	162
CENTER FOR VETERINARY MEDICINE (CVM) .....	163
OFFICE OF ORPHAN PRODUCTS DEVELOPMENT .....	163
OTHER RESEARCH TOPIC(S) WITHIN MISSION OF FDA .....	163
 <u><b>APPENDIX A – INSTRUCTIONS FOR SBIR AND STTR GRANT APPLICATIONS.....</b></u>	 <u><b>A-1</b></u>
 <u><b>APPENDIX B – SBIR PHASE I GRANT APPLICATION FORMS AND REMINDER SHEET .....</b></u>	 <u><b>B-1</b></u>
 <u><b>APPENDIX C – STTR PHASE I GRANT APPLICATION FORMS AND REMINDER SHEET .....</b></u>	 <u><b>C-1</b></u>
 <u><b>APPENDIX D – STTR MODEL AGREEMENT.....</b></u>	 <u><b>D-1</b></u>
 <u><b>APPENDIX E – EXTRAMURAL INVENTION REPORTING COMPLIANCE RESPONSIBILITIES.....</b></u>	 <u><b>E-1</b></u>



## OMNIBUS SOLICITATION OF THE PUBLIC HEALTH SERVICE FOR SMALL BUSINESS INNOVATION RESEARCH (SBIR) AND SMALL BUSINESS TECHNOLOGY TRANSFER RESEARCH (STTR) GRANT APPLICATIONS

### IMPORTANT INFORMATION AND REMINDERS IN THIS SOLICITATION

- **CHANGE IN SBIR/STTR PHASE I AND PHASE II GRANT APPLICATION FORMS.** In late spring of calendar year 2001, pending approval from the Office of Management and Budget, NIH intends to use the revised Public Health Service Grant Application (PHS 398) for SBIR and STTR (Phase I and Phase II) applications. NIH is preparing the revised PHS 398 application for OMB approval. This endeavor is in concert with steps that NIH is taking toward streamlining the grant application procedures. The applications are used to request Federal assistance for research and research-related training. These forms are used by the following PHS agencies: National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Agency for Healthcare Research and Quality (AHRQ), Agency for Toxic Substance and Disease Registry (ATSDR), and The Indian Health Service (IHS).
- **Submissions for April 1, 2001 receipt date.** Applicants planning to submit a Phase I SBIR or Phase I STTR application on or before the April receipt date should use the [SBIR Application Form \(PHS 6246-1\)](#) or the [STTR Application Form \(PHS 6246-3\)](#). See [Appendix A](#) for instructions on completion and submission of these forms.
- **Submissions after April 1, 2001 receipt date.** Applicants planning to submit an SBIR or STTR Phase I or Phase II grant application AFTER April receipt dates should check the NIH Small Business Funding Opportunities website <http://grants.nih.gov/grants/funding/sbir.htm> for more specific details and instructions.
- **CHANGE IN NUMBER OF COPIES.** Submit the original plus five exact, single-sided photocopies of each application.
- **BIOGRAPHICAL SKETCH PAGES.** Biographical sketch pages, limited to 3 pages per person, if necessary, are excluded from the 25-page limitation.
- **RESEARCH PLAN.** Sections A-D are limited to a total of 15 pages, including all tables and diagrams.
- **REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS.** Beginning on October 1, 2000, the NIH will require education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects. Information about this policy may be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>. Frequently Asked Questions ([http://grants.nih.gov/grants/policy/hs\\_educ\\_faq.htm](http://grants.nih.gov/grants/policy/hs_educ_faq.htm)) regarding this policy are also included in this Guide Announcement.
- **PHASE I BUDGET REQUEST THAT EXCEED 6 MONTHS.** Phase I SBIR/STTR Applicants requesting a budget period of more than 1 year (Requests That Exceed the 6-month Guidelines) must prepare applications according to the following instructions <http://grants.nih.gov/grants/funding/sbir.htm#phase1>.

- **SBIR/STTR SOLICITATION AVAILABILITY.** The SBIR/STTR Phase I Grant Solicitation will only be available via electronic means. Printed copies of the Solicitation will not be distributed. Potential applicants are encouraged to check the SBIR/STTR homepage frequently for updates on the program. Any updates or corrections to the solicitation will be posted there.
- **SBIR/STTR SOLICITATION FORMAT.** In an effort to prepare a more succinct and readable document, NIH has changed the format of the SBIR/STTR Phase I Solicitation in order to describe the research or R&D areas of interest for which applications are being solicited while leaving sufficient flexibility in order to obtain the greatest degree of creativity and innovation consistent with the overall objectives of the SBIR/STTR Programs.

**REMINDERS\*\*\*\* REMINDERS\*\*\*\* REMINDERS\*\*\*\* REMINDERS\*\*\*\* REMINDERS\*\*\*\***

- **PHASE I PAGE LIMITATIONS.** SBIR/STTR Phase I applications may not exceed 25 single-spaced standard size (8 ½" x 11") pages, excluding Cover letters; One-page "Introduction" required when submitting a revised (amended) application; Biographical Sketch pages- a change from previous years- (limited to three pages per person, *if necessary*); Letters of commitment from collaborators and consultants; "Checklist" (Form Page 5); "Personal Data on Principal Investigator" Form Page; and, if applicable, Page(s) furnishing information required under "Prior SBIR/STTR Phase II Awards. The 25-page limit includes all other Form Pages and "continuation" pages suggested by the instructions.
- **TYPE SIZE SPECIFICATIONS.** The height of the letters must not be smaller than 10 point; type density must be no more than 15 characters per inch (cpi); there must be no more than 6 lines of type within a vertical inch. The type size used throughout the application must conform to ALL of these requirements. APPLICATIONS NOT MEETING THESE REQUIREMENTS WILL BE RETURNED WITHOUT REVIEW.
- **SINGLE OMNIBUS SOLICITATION FOR GRANT APPLICATIONS AND COINCIDENT RECEIPT DATES FOR SBIR/STTR GRANT APPLICATIONS.** Since the similarities between the NIH SBIR and STTR Grant Solicitations, both in research topics that may be of interest to small businesses and in application instructions, a single Omnibus Solicitation of the NIH, CDC, and FDA for SBIR/STTR Grant Applications has been issued for CY 2001 for coincident grant application receipt dates.
- **SPECIAL ANNOUNCEMENTS (Program Announcements/Requests for Applications) FOR SMALL BUSINESS RESEARCH OPPORTUNITIES.** Subscribe to the weekly content notifications via email using the NIH Guide Table of Contents Notification LISTSERV service (<http://grants.nih.gov/grants/guide/listserv.htm>.)

## I. GENERAL PROGRAM DESCRIPTION

The Small Business Innovation Research (SBIR) program was established by the Small Business Research and Development Enhancement Act of 1992. Under this program, agencies of the Public Health Service (PHS), Department of Health and Human Services (HHS), and certain other Federal agencies are required to reserve 2.5% of their current fiscal year extramural budgets for small companies to conduct research or research and development (R/R&D).

The Small Business Technology Transfer (STTR) program, currently in five Federal agencies, was established by the Small Business Technology Transfer Act of 1992 (Public Law 102-564, Title II). Under this program, 0.15% of a Federal agency's extramural R/R&D effort is reserved for awards to small business concerns and their non-profit research institution partners for cooperative research and development efforts.

The objectives of the SBIR Program include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal R/R&D needs, increasing private sector commercialization of innovations developed through Federal SBIR R&D, increasing small business participation in Federal R/R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned business concerns in the SBIR program.

The STTR program further expands the goals through cooperative research and development carried out between small business concerns and research institutions.

The National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and Food and Drug Administration (FDA) invite eligible small business concerns to submit Phase I applications for the Calendar Year (CY) 2001 Small Business Innovation Research (SBIR) program and, applicable to NIH only, for the CY 2001 Small Business Technology Transfer (STTR) program.

Beginning in CY 2000, NIH issued a single Omnibus Solicitation of the NIH, CDC, and FDA for SBIR/STTR Grant Applications. Accordingly, a single Omnibus Solicitation of the NIH, CDC,

and FDA for SBIR/STTR Grant Applications will be issued for CY 2001 grant application receipt dates.

**NOTE: The CDC and FDA participate ONLY in the SBIR program.**

This single SBIR/STTR solicitation (PHS 2001-2) provides information about each program. The significant difference between the SBIR and STTR programs is that the STTR requires the small business concern to have a formal collaboration with researchers at universities and other non-profit research institutions and play a significant intellectual role in the conduct of each STTR project. Also, unlike the SBIR Program, there is no stipulation under the STTR program that the Principal Investigator (PI) must have his/her primary employment with the small business concern. Therefore, the PI on an STTR may be from the small business concern or the research institution as long as s/he has a formal appointment with or commitment to the applicant small business concern, which is characterized by an official relationship between the small business concern and that individual.

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### A. SBIR/STTR PROGRAMS: THREE PHASES

<b>PHASE I: Feasibility</b> \$100,000 6 Months (SBIR) 1 Year (STTR)
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The objective of Phase I is to establish the technical/scientific merit and feasibility of the proposed R/R&D

efforts and to determine the quality of performance of the small business grantee organization prior to providing further Federal support in Phase II. Preliminary data are not required. SBIR Phase I awards normally may not exceed \$100,000 total costs (direct costs, indirect costs, and negotiated fixed fee) for a period normally not to exceed 6 months. STTR Phase I awards normally may not exceed \$100,000 total costs for a period of 1 year. For SBIR projects, the total amount of all contractual costs and consultant fees normally may not exceed 33% of the total costs requested. However, these award levels for time and amount are statutory guidelines, not ceilings. Therefore, applicants are encouraged to propose a budget and project period that is appropriate for completion of the research

project. Deviations from the guidelines are acceptable, *but must be well justified*.

**Applicants are encouraged to discuss budgetary deviations with NIH program staff prior to submission of the application.**

SBIR Phase I applications should be prepared using PHS 6246-1 forms and in accordance with SBIR instructions in Section XI. STTR Phase I applications should be prepared using PHS 6246-3 forms and in accordance with STTR instructions in Section XI. Evaluation and selection criteria are described in Section VI.

A Phase I Final Report is required for the completion of a Phase I SBIR/STTR project. All Phase I Final Reports should be prepared in accordance with the instructions in Section VII.

**PHASE II: Full R/R&D Effort**

~ \$750,000 (SBIR)  
~ \$500,000 (STTR)  
~ 2 Years

The objective of Phase II is to continue the research or R&D efforts initiated in

Phase I. Funding shall be based on the results of Phase I, scientific and technical merit, and commercial potential of the Phase II application. SBIR Phase II awards normally may not exceed \$750,000 in total costs (direct costs, indirect costs, and negotiated fixed fee) for a period normally not to exceed 2 years. STTR Phase II awards normally may not exceed \$500,000 total costs (direct costs, indirect costs, and negotiated fixed fee) for a period normally not to exceed 2 years. However, these award levels for time and amount are statutory guidelines, not ceilings. Therefore, applicants are encouraged to propose a budget and project period that is appropriate for completion of the research project. Deviations from the guidelines are acceptable, *but must be well justified*.

**Applicants are encouraged to discuss budgetary deviations with NIH program staff prior to submission of the application.**

Only Phase I grantees are eligible to obtain Phase II funding, and only one Phase II award may be made for a single SBIR/STTR project. Phase II applications may be submitted either before or after expiration of the Phase I budget period, except for those applicants electing to submit Phase I and Phase II applications concurrently under the Fast-Track procedures (described in Section VI, item G).

Also, under special circumstances, requests for supplemental funds to existing Phase I grants or

requests for an extension of the period of support with funds, may be considered. (*The awarding of supplemental funds applies to NIH ONLY, as CDC and FDA do not make awards greater than the stated guidelines.*)

**PHASE III: Commercialization  
No SBIR/STTR Funds**

The objective of Phase III, where appropriate, is for the small business

concern to pursue with non-SBIR/STTR funds (either Federal or non-Federal) the commercialization objectives resulting from the results of the research or R&D funded in Phases I and II. In some Federal agencies, Phase III may involve follow-on, non-SBIR/STTR funded R&D, or production contracts for products or processes intended for use by the U.S. Government.

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## B. FAST-TRACK APPLICATIONS

**Fast Track Applications: PHASE I + II**

Parallel review option  
Phase I and Phase II submitted together  
Product Development Plan

The NIH Fast-Track mechanism expedites the decision and award

of SBIR and STTR Phase II funding for scientifically meritorious applications that have a high potential for commercialization. Fast Track incorporates a parallel review option, in which both Phase I and Phase II grant applications are submitted and reviewed together. As with other Phase I applications, preliminary data are not required. However, the Phase I portion of a Fast Track must specify clear, measurable goals (milestones) that should be achieved prior to initiating Phase II work. In addition, a Fast Track application must present a Product Development Plan that addresses specific points. Instructions on the preparation of a Fast Track application may be found in Section VI. G.

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## C. PURPOSE OF SOLICITATION

The purpose of this Solicitation is to invite Phase I grant applications from domestic small business concerns that have the technological expertise to contribute to the R&D mission(s) of the NIH, CDC, and FDA awarding components identified in the solicitation, and to provide to those applicants choosing the Fast-Track review option the opportunity to submit Phase II grant applications concurrently with Phase I

applications. The CDC and FDA do not participate in the STTR program.

This solicitation outlines the objectives of the agencies' SBIR/STTR grants program, the eligibility requirements for those small business concerns wishing to participate, and the application and review processes.

The research topics shown in the solicitation represent program areas that may be of interest to applicant small business concerns in the development of projects that have the potential for commercialization. Small business concerns are encouraged to submit SBIR/STTR grant applications in these areas.

**NOTE: SBIR/STTR grant applications will be accepted and considered in any area within the mission of the awarding components identified in this solicitation.**

Applicants are strongly encouraged to query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, and FDA awarding components.

Additional information on each of the awarding components and their research interests is available electronically on the home pages shown throughout the "Research Topics" section of the solicitation.

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## D. SBIR/STTR PROGRAM ELIGIBILITY

### Organizational Criteria

Each organization submitting a grant application under the SBIR/STTR program must qualify as a small business concern in accordance with the definition given in Section III. In determining whether an applicant is a small business concern, an assessment will be made of several factors, including whether or not it is independently owned and operated and whether or not it is an affiliate of a larger organization whose employees, when added to those of the applicant organization, exceed 500. In conducting this assessment, all appropriate factors will be considered, including common ownership, common management, and contractual relationships.

In accordance with Title 13 Code of Federal Regulations (CFR) Part 121.3, affiliation exists when either directly or indirectly "(i).one concern controls or has the power to control the other, or

(ii) a third party or parties controls or has the power to control both." One of the circumstances that would lead to a finding that an organization is controlling or has the power to control another organization involves sharing common office space and/or employees and/or other facilities (e.g., laboratory space). 13 CFR 121.3 also states that control or the power to control exists when "key employees of one concern organize a new concern ... and serve as its officers, directors, principal stockholders, and/or key employees, and one concern is furnishing or will furnish the other concern with subcontracts, financial or technical assistance, and/or other facilities, whether for a fee or otherwise."

Where there is indication of sharing of common employees, a determination will be made on a case-by-case basis of whether such sharing constitutes control or the power to control.

All SBIR/STTR grant applications will be examined with the above considerations in mind. If it appears that an applicant organization does not meet eligibility requirements, the PHS will request a size determination of the organization from the cognizant Small Business Administration (SBA) regional office. Under these circumstances in which eligibility is unclear, no SBIR or STTR award will be made until a determination is provided by the SBA.

### SBIR/STTR Eligibility Checkpoint

- ☒ For-profit U.S. business firm.
- ☒ At least 51% U.S.- owned and independently operated.
- ☒ Small Business located in the U.S.
- ☒ Principal Investigator's primary employment with small business during project (SBIR only).
- ☒ 500 or fewer employees.

### Performance of Research and Analytical Work by the Applicant Organization

#### SBIR

In Phase I, normally, a minimum of two-thirds or 67% of the research or analytical effort must be carried out by the small business concern.

Therefore, consultant fees and contracts to third parties for portions of the scientific/technical

effort generally may not exceed 33% of the total budget, including direct costs, indirect costs, and fixed fee. The basis for determining the percentage of work to be performed by each of the cooperative parties will be the total of direct and indirect costs attributable to each party, UNLESS OTHERWISE DESCRIBED AND JUSTIFIED IN THE "CONTRACTUAL ARRANGEMENTS" PORTION OF THE "RESEARCH PLAN" SECTION OF THE APPLICATION.

In Phase II, normally, a minimum of one-half or 50% of the research or analytical effort must be carried out by the small business concern.

Therefore, consultant fees and contracts to third parties for portions of the scientific/technical effort generally may not exceed 50% of the total budget, including direct costs, indirect costs, and fixed fee. The basis for determining the percentage of work to be performed by each of the cooperative parties will be the total of direct and indirect costs attributable to each party, UNLESS OTHERWISE DESCRIBED AND JUSTIFIED IN THE "CONTRACTUAL ARRANGEMENTS" PORTION OF THE "RESEARCH PLAN" SECTION OF THE APPLICATION.

The research and analytical work performed by the grantee organization is to be conducted in research space occupied by, available to, and under the control of the SBIR/STTR grantee for the conduct of its portion of the proposed project. However, when required by the project activity, access to special facilities or equipment in another organization is permitted, as in cases where the SBIR/STTR awardee has entered into a sub-contractual agreement with another institution for a specific, limited portion of the research project.

Whenever a proposed SBIR/STTR project is to be conducted in facilities other than those of the applicant organization, and if the application has the likelihood for funding, the awarding component will request that the small business concern provide a letter from the organization stating that leasing/rental arrangements have been negotiated for appropriate research space (i.e., space that will be available to and under the control of the SBIR/STTR grantee organization). This letter, to be signed by an authorized official of the organization whose facilities are to be used for the SBIR/STTR project, must certify that the small business concern will have unlimited access to and

control over the research space. In addition, the letter must include a description of the facilities and, if appropriate, equipment that will be leased/rented to the grantee organization.

## **STTR**

In Phase I and Phase II, at least 40% of the work must be performed by the small business concern and at least 30% of the work must be performed by the Research Institution. The basis for determining the percentage of work to be performed by each of the cooperative parties will be the total of direct and indirect costs attributable to each party UNLESS OTHERWISE DESCRIBED AND JUSTIFIED IN THE "CONTRACTUAL ARRANGEMENTS" PORTION OF THE "RESEARCH PLAN" SECTION OF THE APPLICATION.

## **Performance Site Criteria**

For both SBIR/STTR Phase I and Phase II, the research or R&D project activity must be performed in its entirety in the United States (see Section III, Definitions). In those rare circumstances that necessitate the use of foreign sites (e.g., patient populations) because of the study design, investigators must thoroughly justify the use of these sites in the application. Similarly, in those rare circumstances that necessitate the purchase of materials from other countries, investigators must thoroughly justify the request. These rare situations will be considered on a case-by-case basis. While the SBIR/STTR research or R&D project activity must be performed in its entirety in the United States, other work outside of the United States, which is necessary to the overall completion of the project, could be supported by non-SBIR/STTR funds.

## **Principal Investigator Criteria**

### **SBIR**

The primary employment of the Principal Investigator must be with the small business concern at the time of award and during the conduct of the proposed project. Primary employment means that more than one half of the Principal Investigator's time is spent in the employ of the small business concern. Primary employment with a small business concern precludes full-time employment at another organization.

As defined in 42 CFR 52, the Principal Investigator is the “single individual designated by the grantee in the grant application ... who is responsible for the scientific and technical direction of the project.” When the proposed Principal Investigator clearly does not have sufficient qualifications to assume this role, the application is not likely to receive a favorable evaluation (see Section VII, Method of Selection and Evaluation Criteria).

If the application has the likelihood for funding, the awarding component will require documentation to verify the eligibility of the Principal Investigator. This will be necessary when, at the time of submission of the application, the Principal Investigator (1) is a less-than-full-time employee of the small business concern; (2) is concurrently employed by another organization; or (3) gives the appearance of being concurrently employed by another organization, whether for a paid or unpaid position.

That is to say, if the Principal Investigator is employed or appears to be employed by an organization other than the applicant organization in a capacity such as Research Fellow, Consultant, Adjunct Professor, Clinical Professor, Clinical Research Professor, or Associate, a letter must be provided by each employing organization confirming that, if an SBIR grant is awarded to the applicant small business concern, the Principal Investigator is or will become a less-than-half-time employee of such organization and will remain so for the duration of the SBIR project. If the Principal Investigator is employed by a university, such a letter must be provided by the Dean's office or equivalent; for other organizations, the letter must be signed by a corporate official.

This requirement applies also to those individuals engaged currently as the Principal Investigator on an active SBIR project. All current employment and all other appointments of the Principal Investigator must be identified in his or her “Biographical Sketch” required as part of the application. Be certain that correct beginning and ending dates are indicated for each employment record listed.

### **STTR**

The Principal Investigator must have a formal appointment with or commitment to the applicant small business concern, which is characterized

by an official relationship between the small business concern and that individual. Such a relationship does not necessarily involve a salary or other form of remuneration. In all cases, however, the Principal Investigator's official relationship with the grantee must entail sufficient opportunity for the Principal Investigator to carry out his or her responsibilities for the overall scientific and technical direction of the project. Documentation describing the official relationship of the Principal Investigator with the applicant small business concern should NOT be submitted with the grant application, but a copy must be furnished upon the request of the NIH awarding component.

**Note: Signatures on the face page and the Research Institution budget page certify that the Principal Investigator has a formal relationship with/commitment to the small business concern.**

Following are examples of situations describing the official relationship of the Principal Investigator with the applicant small business organization:

- A Principal Investigator with a full-time, university appointment may also have appointments (with or without salary) and still appropriately consider his or her commitment to the university to be “full-time,” consistent with the personnel policies and procedures of the university applied on a routine basis. The Principal Investigator's commitment to the university and other organizations (including the applicant small business concern) cannot exceed 100% of his or her total professional effort.
- A Principal Investigator with a full-time, 12-month appointment with a small business concern would be considered to have a commitment to the applicant organization of 100% of his or her total professional effort.
- A Principal Investigator who has a part-time appointment with a small business concern and has concurrent commitments or appointments with organizations in addition to the small business concern would deem each commitment as a portion of 100% of his or her total professional effort.

As responsible stewards of funds, the NIH is concerned that the Principal Investigator has the time available to carry out the proposed STTR

research activities. Therefore, the Principal Investigator should take care to assure peer reviewers and NIH staff that the time proposed for a particular project is reasonable and that he or she has sufficient time (minimum 10% effort) available from among his or her total professional commitments to devote to this project.

## II. AGENCY CONTACT FOR INFORMATION

The SBIR/STTR Phase I Grant Solicitation will ***only be available via electronic means.*** Printed copies of the Solicitation will not be distributed. The SBIR/STTR Phase I Grant Solicitation and the Phase II Grant Application package, both text and forms, are available electronically on the NIH's "Small Business Funding Opportunities" home page at <http://grants.nih.gov/grants/funding/sbir.htm>.

### Program Officials/Agency Contact Information

Applicants are strongly encouraged to contact NIH program staff prior to submitting an SBIR/STTR grant application for information regarding research topics. The names, addresses, and communication numbers of other contacts as well as Internet websites for

each PHS awarding component are included in Section X, Program Descriptions/Research

Topics. More detailed information on each of the NIH awarding components, as well as the CDC and FDA, and their research interests are available electronically on the home pages cited in the table and in Section X. For administrative and business management questions that are not answered in this solicitation, a grants management contact is identified.

Questions of a general nature about the NIH SBIR/STTR program should be directed to:

Ms. Jo Anne Goodnight  
NIH SBIR/STTR Program Coordinator  
6701 Rockledge Drive  
Rockledge II, Room 6186  
Bethesda, MD 20892-7911  
Phone: 301-435-2688 Fax: 301-480-0146  
Email: [jq128w@nih.gov](mailto:jq128w@nih.gov)

or

PHS SBIR/STTR Solicitation Office  
13687 Baltimore Avenue  
Laurel, MD 20707-5096  
Phone: (301) 206-9385  
Fax: (301) 206-9722  
E-mail: [sbirsttr@peacetech.com](mailto:sbirsttr@peacetech.com)

The following table includes points of contact information for each PHS awarding component.

AWARDING COMPONENT/AGENCY CONTACT INFORMATION		
AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute on Aging <a href="http://www.nih.gov/nia">http://www.nih.gov/nia</a>	Dr. Miriam F. Keltz Phone: 301-496-9322 Fax: 301-402-2945 Email: <a href="mailto:mk46u@nih.gov">mk46u@nih.gov</a>	Ms. Linda Whipp Phone: 301-496-1472 Fax: 301-402-3672 Email: <a href="mailto:lw17m@nih.gov">lw17m@nih.gov</a>
National Institute on Alcohol Abuse and Alcoholism <a href="http://www.niaaa.nih.gov">http://www.niaaa.nih.gov</a>	Dr. Michael Eckardt Phone: 301-443-6107 Fax: 301-443-6077 Email: <a href="mailto:me25t@nih.gov">me25t@nih.gov</a>	Ms. Linda Hilley Phone: 301-443-4704 Fax: 301-443-3891 Email: <a href="mailto:lh67b@nih.gov">lh67b@nih.gov</a>
National Institute of Allergy and Infectious Diseases <a href="http://www.niaid.nih.gov">http://www.niaid.nih.gov</a>	Dr. Gregory Milman Phone: 301-496-8666 Fax: 301-402-0369 Email: <a href="mailto:gm16s@nih.gov">gm16s@nih.gov</a>	Ms. Mary Kirker Phone: 301-496-7231 Fax: 301-480-3780 Email: <a href="mailto:mk35h@nih.gov">mk35h@nih.gov</a>

AWARDING COMPONENT/AGENCY CONTACT INFORMATION		
AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute of Arthritis and Musculoskeletal and Skin Diseases <a href="http://www.nih.gov/niams">http://www.nih.gov/niams</a>	Dr. Steven J. Hausman Phone: 301-594-2463 Fax: 301-480-4543 Email: <a href="mailto:sh41g@nih.gov">sh41g@nih.gov</a>	Ms. Florence Turska Phone: 301-594-3507 Fax: 301-480-5450 Email: <a href="mailto:ft7p@nih.gov">ft7p@nih.gov</a>
National Cancer Institute <a href="http://www.nci.nih.gov">http://www.nci.nih.gov</a>	Ms. Kay Etzler Phone: 301-496-1550 Fax: 301-496-7807 Email: <a href="mailto:etzlerk@mail.nih.gov">etzlerk@mail.nih.gov</a>	Ms. Kathleen Shino Phone: 301-846-1016 Fax: 301-846-1198 Email: <a href="mailto:ks48e@nih.gov">ks48e@nih.gov</a>
National Institute of Child Health and Human Development <a href="http://www.nichd.nih.gov">http://www.nichd.nih.gov</a>	Dr. Louis A. Quatrano Phone: 301-402-2242 Fax: 301-402-0832 Email: <a href="mailto:lq2n@nih.gov">lq2n@nih.gov</a>	Ms. Diane Watson Phone: 301-435-6975 Fax: 301-402-0915 Email: <a href="mailto:dw40j@nih.gov">dw40j@nih.gov</a>
National Institute on Drug Abuse <a href="http://www.nida.nih.gov">http://www.nida.nih.gov</a>	Dr. Cathrine Sasek Phone: 301-443-1056 Fax: 301-443-6277 Email: <a href="mailto:csasek@nih.gov">csasek@nih.gov</a>	Mr. Gary Fleming Phone: 301-443-6710 Fax: 301-594-6847 Email: <a href="mailto:gfs@nih.gov">gfs@nih.gov</a>
National Institute on Deafness and Other Communication Disorders <a href="http://www.nih.gov/nidcd">http://www.nih.gov/nidcd</a>	Dr. Lynn E. Luethke Phone: 301-402-3458 Fax: 301-402-6251 Email: <a href="mailto:lh99s@nih.gov">lh99s@nih.gov</a>	Ms. Sharon Hunt Phone: 301-402-0909 Fax: 301-402-1758 Email: <a href="mailto:sh79f@nih.gov">sh79f@nih.gov</a>
National Institute of Dental and Craniofacial Research <a href="http://www.nidcr.gov">http://www.nidcr.gov</a>	Dr. Eleni Kousvelari Phone: 301-594-2427 Fax: 301-480-8318 Email: <a href="mailto:Eleni.Kousvelari@nih.gov">Eleni.Kousvelari@nih.gov</a>	Mr. Martin Rubinstein Phone: 301-594-4800 Fax: 301-480-8301 Email: <a href="mailto:mr49c@nih.gov">mr49c@nih.gov</a>
National Institute of Diabetes and Digestive and Kidney Diseases <a href="http://www.niddk.nih.gov">http://www.niddk.nih.gov</a>	Dr. Judith Podskalny Phone: 301-594-8876 Fax: 301-480-8300 Email: <a href="mailto:jp53s@nih.gov">jp53s@nih.gov</a>	Mr. George Tucker Phone: 301-594-8853 Fax: 301-480-3504 Email: <a href="mailto:gt35v@nih.gov">gt35v@nih.gov</a>
National Institute of Environmental Health Sciences <a href="http://www.niehs.nih.gov">http://www.niehs.nih.gov</a>	Dr. Jerrold Heindel Phone: 919-541-0781 Fax: 919-541-5064 Email: <a href="mailto:jh190f@nih.gov">jh190f@nih.gov</a>	Ms. Carolyn Winters Phone: 919-541-7823 Fax: 919-541-2860 Email: <a href="mailto:cw47d@nih.gov">cw47d@nih.gov</a>
National Eye Institute <a href="http://www.nei.nih.gov">http://www.nei.nih.gov</a>	Dr. Ralph Helmsen Phone: 301-496-5301 Fax: 301-402-0528 Email: <a href="mailto:rh27v@nih.gov">rh27v@nih.gov</a>	Mr. William Darby Phone: 301-496-5884 Fax: 301-496-9997 Email: <a href="mailto:wwd@nei.nih.gov">wwd@nei.nih.gov</a>
National Institute of General Medical Sciences <a href="http://www.nih.gov/nigms">http://www.nih.gov/nigms</a>	Dr. Peter Preusch Phone: 301-594-1832 Fax: 301-480-2802 Email: <a href="mailto:pp27g@nih.gov">pp27g@nih.gov</a>	Ms. Linda Roberts Phone: 301-594-5141 Fax: 301-480-1969 Email: <a href="mailto:lr24v@nih.gov">lr24v@nih.gov</a>
National Heart, Lung, and Blood Institute <a href="http://www.nhlbi.nih.gov">http://www.nhlbi.nih.gov</a>	Dr. John T. Watson Phone: 301-435-0513 Fax: 301-480-1336 Email: <a href="mailto:jw53f@nih.gov">jw53f@nih.gov</a>	Mr. Ed Donohue Phone: 301-435-0144 Fax: 301-480-3310 Email: <a href="mailto:ed25b@nih.gov">ed25b@nih.gov</a>

AWARDING COMPONENT/AGENCY CONTACT INFORMATION		
AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Human Genome Research Institute <a href="http://www.nhgri.nih.gov">http://www.nhgri.nih.gov</a>	Dr. Bettie J. Graham Phone: 301-496-7531 Fax: 301-480-2770 Email: <a href="mailto:bg30t@nih.gov">bg30t@nih.gov</a>	Ms. Jean Cahill Phone: 301-402-0733 Fax: 301-402-1951 Email: <a href="mailto:jc166o@nih.gov">jc166o@nih.gov</a>
National Institute of Mental Health <a href="http://www.nimh.nih.gov">http://www.nimh.nih.gov</a>	Dr. Michael F. Huerta Phone: 301-443-5625 Fax: 301-443-1731 Email: <a href="mailto:mh38f@nih.gov">mh38f@nih.gov</a>	Mr. Michael Loewe Phone: 301-435-7008 Fax: 301-402-0915 Email: <a href="mailto:ml70m@nih.gov">ml70m@nih.gov</a>
National Institute of Neurological Disorders and Stroke <a href="http://www.ninds.nih.gov">http://www.ninds.nih.gov</a>	Dr. Thomas Miller Phone: 301-496-1779 Fax: 301-402-1501 Email: <a href="mailto:tm208y@nih.gov">tm208y@nih.gov</a>	Ms. Kathleen Howe Phone: 301-496-9231 Fax: 301-402-0219 Email: <a href="mailto:kh52x@nih.gov">kh52x@nih.gov</a>
National Institute of Nursing Research <a href="http://www.nih.gov/ninr">http://www.nih.gov/ninr</a>	Dr. Hilary Sigmon Phone: 301-594-5970 Fax: 301-480-8260 Email: <a href="mailto:hs38k@nih.gov">hs38k@nih.gov</a>	Ms. Cindy McDermott Phone: 301-594-6869 Fax: 301-480-8260 Email: <a href="mailto:cm253t@nih.gov">cm253t@nih.gov</a>
National Center for Research Resources <a href="http://www.ncrr.nih.gov">http://www.ncrr.nih.gov</a>	Dr. Louise E. Ramm Phone: 301-435-0879 Fax: 301-480-3658 Email: <a href="mailto:lr34m@nih.gov">lr34m@nih.gov</a>	Mr. Bryan Clark Phone: 301-435-0844 Fax: 301-480-3777 Email: <a href="mailto:ClarkB@ncrr.nih.gov">ClarkB@ncrr.nih.gov</a>
National Center for Complementary and Alternative Medicine <a href="http://nccam.nih.gov">http://nccam.nih.gov</a>	Dr. Richard Nahin Phone: 301-496-4792 Fax: 301-402-4741 Email: <a href="mailto:rn8p@nih.gov">rn8p@nih.gov</a>	Ms. Suzanne White Phone: 301-435-0171 Fax: 301-480-3310 Email: <a href="mailto:sw52h@nih.gov">sw52h@nih.gov</a>
National Library of Medicine <a href="http://www.nlm.nih.gov">http://www.nlm.nih.gov</a>	Mr. Milton Corn Phone: 301-496-4621 Fax: 301-402-0421 Email: <a href="mailto:pc49n@nih.gov">pc49n@nih.gov</a>	Mr. John Seachrist Phone: 301-496-4221 Fax: 301-402-0421 Email: <a href="mailto:js132f@nih.gov">js132f@nih.gov</a>
Centers for Disease Control and Prevention (CDC) <a href="http://www.cdc.gov">http://www.cdc.gov</a>	Ms. Nina Waters Phone: 770-488-2805 Fax: 770-488-2847 Email: <a href="mailto:jvw0@cdc.gov">jvw0@cdc.gov</a>	Ms. Joanne Wojcik Phone: 770-488-2717 Fax: 770-488-2777 Email: <a href="mailto:jcw6@cdc.gov">jcw6@cdc.gov</a>
Food and Drug Administration (FDA) <a href="http://www.fda.gov">http://www.fda.gov</a>	Ms. Rosemary Springer Phone: 301-827-7182 Fax: 301-827-7106 Email: <a href="mailto:rspringe@oc.fda.gov">rspringe@oc.fda.gov</a>	Ms. Olia Hopkins Phone: 301-827-7150 Fax: 301-827-7106 Email: <a href="mailto:ohopkins@oc.fda.gov">ohopkins@oc.fda.gov</a>

### III. DEFINITIONS

**Commercialization.** The process of developing markets and producing and delivering products for sale (whether by the originating party or by others); as used here, commercialization includes both government and private sector markets.

**Collaborator.** An individual involved with the Principal Investigator in the scientific development or execution of the project. These individuals would typically devote a specific percent of effort to the project and would be identified as key personnel. The collaborator may be employed by, or affiliated with, either the grantee organization or an organization participating in the project under a consortium or contractual agreement.

**Consortium or Contractual Agreement.** An agreement whereby a research project is carried out by the grantee and one or more other organizations that are separate legal entities. In this arrangement, the grantee contracts for the performance of a substantial and/or significant portion of the activities to be conducted under the grant. These agreements typically involve a specific percent of effort from the consortium organization's Principal Investigator and a categorical breakdown of costs, such as personnel, supplies, and other allowable expenses, including indirect costs.

**Consultant.** An individual hired to give professional advice or services for a fee, normally not as an employee of the hiring party. Consultants may also include firms that provide paid professional advice or services.

**Contract.** An award instrument establishing a binding legal procurement relationship between a funding agency and the recipient, obligating the latter to furnish an end product or service and binding the agency to provide payment therefore.

**Cooperative Agreement.** A financial assistance mechanism to be used in lieu of a grant when substantial Federal programmatic involvement with the recipient during performance is anticipated by the PHS awarding component.

**Essentially Equivalent Work.** This term is meant to identify "scientific overlap," which occurs when (1) substantially the same research is proposed for funding in more than one proposal (contract proposal or grant application) submitted to the same Federal agency; OR (2) substantially the same research is submitted to two or more different Federal agencies for review and funding consideration; OR (3) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more proposals or awards, regardless of the funding source.

**Feasibility.** The extent to which a study or project may be done practically and successfully.

**Grant.** A financial assistance mechanism whereby money and/or direct assistance is provided to carry out approved activities.

**Innovation.** Something new or improved, including research for (1) development of new

technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For the purposes of PHS programs, an example of "innovation" would be new medical or biological products, for improved value, efficiency, or costs.

**Key Personnel Engaged on Project.** This term is meant to identify those individuals who contribute in a substantive way to the scientific development or execution of the project, whether or not salaries are requested.

**Principal Investigator.** The one individual designated by the applicant organization to direct the project or program to be supported by the grant. The Principal Investigator is responsible and accountable for the proper conduct of the project or program.

**Program Income.** Gross income earned by a grant recipient during the budget period of the grant as a result of activities supported by the grant award. The *NIH Grants Policy Statement* (<http://grants.nih.gov/grants/policy/nihgps>) contains a detailed explanation of program income, ways in which it may be generated and accounted for, and the various options for its use and disposition.

Examples of program income include:

- Patent or copyright royalties.
- Fees earned from services performed under the grant, such as those resulting from laboratory drug testing.
- Rental or usage fees, such as those earned from fees charged for use of computer equipment purchased with grant funds.
- Third-party patient reimbursement for hospital or other medical services, such as insurance payments for patients when such reimbursement occurs because of the grant-supported activity.
- Funds generated by the sale of products developed under the grant, which include but are not limited to drugs, assays, devices, instrumentation, software, laboratory techniques/methodologies, and testing/training devices or systems.

- Funds generated by the sale of commodities, such as tissue cultures, cell lines, or research animals.

Generally, SBIR/STTR grantee organizations that earn program income may be authorized to have such income added to the grant account and used to further the objectives of the research project. Authorization must be requested from the Grants Management Officer of the appropriate PHS awarding component.

**Prototype.** A model of something to be further developed and includes designs, protocols, questionnaires, software, devices, etc.

**Research Institution.** A United States research organization that is:

- A nonprofit college or university OR
- A nonprofit research institution, including nonprofit medical and surgical hospitals. (A “nonprofit institution” is defined as an organization that is owned and operated exclusively for scientific or educational purposes, no part of the net earnings of which inures to the benefit of any private shareholder or individual.) OR
- A contractor-operated, federally funded research and development center, as identified by the National Science Foundation in accordance with the Government-wide Federal Acquisition Regulation issued in accordance with section 35(c)(1) of the Office of Federal Procurement Policy Act (or any successor legislation thereto).

(Laboratories staffed by Federal employees do not meet the definition of “research institution” for purposes of the STTR program.)

**Research or Research and Development (R/R&D).** Any activity that is:

- A systematic, intensive study directed toward greater knowledge or understanding of the subject studied.
- A systematic study directed specifically toward applying new knowledge to meet a recognized need.

- A systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

**Small Business Concern.** A small business concern is one that, at the time of award of Phase I and Phase II, meets the following criteria:

1. Is independently owned and operated, is not dominant in the field of operation in which it is proposing, has its principal place of business located in the United States, and is organized for profit.
2. Is at least 51% owned, or in the case of a publicly owned business, at least 51% of its voting stock is owned by United States citizens or lawfully admitted permanent resident aliens.
3. Has, including its affiliates, a number of employees not exceeding 500, and meets the other regulatory requirements found in 13 CFR Part 121. Business concerns, other than investment companies licensed, or state development companies qualifying under the Small Business Investment Act of 1958, 15 U.S.C. 661, et seq., are affiliates of one another when either directly or indirectly, (a) one concern controls or has the power to control the other; or (b) a third-party/parties controls or has the power to control both.

Control can be exercised through common ownership, common management, and contractual relationships. The term “affiliates” is defined in greater detail in 13 CFR 121.3-2(a). The term “number of employees” is defined in 13 CFR 121.3-2(t).

Business concerns include, but are not limited to, any individual (sole proprietorship), partnership, corporation, joint venture, association, or cooperative. Further information may be obtained by contacting the Small Business Administration Size District Office at <http://www.sba.gov/size/>.

**Socially and Economically Disadvantaged Individual.** A member of any of the following groups:

1. Black Americans

2. Hispanic Americans
3. Native Americans
4. Asian-Pacific Americans
5. Subcontinent Asian Americans
6. Other groups designated from time to time by SBA to be socially disadvantaged
7. Any other individual found to be socially and economically disadvantaged by SBA pursuant to Section 8(a) of the Small Business Act, 15 U.S.C. 637(a)

***Socially and Economically Disadvantaged Small Business Concern.*** A socially and economically disadvantaged small business concern:

1. Is one that is at least 51% owned by (a) an Indian tribe or a native Hawaiian organization, or (b) one or more socially and economically disadvantaged individuals; AND
2. Whose management and daily business operations are controlled by one or more socially and economically disadvantaged individuals.

***Subcontract.*** Any agreement, other than one involving an employer-employee relationship, entered into by a Federal Government prime contractor calling for supplies or services required solely for the performance of the prime contract or another subcontract.

***United States.*** The 50 states, territories and possessions of the U.S., Commonwealth of Puerto Rico, Trust Territory of the Pacific Islands, and District of Columbia.

***Women-Owned Small Business Concern.*** A small business concern that is at least 51% owned by a woman or women who also control and operate it. "Control" in this context means exercising the power to make policy decisions. "Operate" in this context means being actively involved in the day-to-day management.

#### IV. GRANT APPLICATION PREPARATION INSTRUCTIONS AND REQUIREMENTS

REFER TO "SPECIFIC GRANT APPLICATION PREPARATION INSTRUCTIONS AND REQUIREMENTS" FOR MORE DETAILED INFORMATION IN THE PREPARATION OF YOUR GRANT APPLICATION.

**In late spring of calendar year 2001, pending approval from the Office of Management and Budget, NIH intends to use the revised Public Health Service Grant Application (PHS 398) for SBIR and STTR (Phase I and Phase II) applications submitted to NIH, CDC and FDA.**

This endeavor is in concert with steps that NIH is taking toward streamlining the grant application procedures. The PHS 398 application is used to request Federal assistance for research and research-related training. These forms are used by the following PHS agencies: National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Agency for Healthcare Research and Quality (AHRQ), Agency for Toxic Substance and Disease Registry (ATSDR), and The Indian Health Service (IHS).

- Applicants planning to submit a Phase I SBIR or STTR application *prior to April* should use the *SBIR Application Form (PHS 6246-1)* or the *STTR Application Form (PHS 6246-3)*. These forms, as well as instructions for completion and submission, are available electronically at <http://grants.nih.gov/grants/funding/sbirsttr1/index.htm>.
- Applicants planning to submit an SBIR or STTR Phase I or Phase II grant application after April receipt dates should check the NIH Small Business Funding Opportunities website <http://grants.nih.gov/grants/funding/sbir.htm> for more specific details and instructions.

Potential applicants are strongly encouraged to contact program staff (see Section X) for pre-application guidance and/or for more specific information on the research topics described in this solicitation.

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#### A. LIMITATIONS ON LENGTH OF APPLICATION

Observe the page number limitations or the application will be returned without review.

1. SBIR/STTR Phase I applications may not exceed 25 single-spaced standard size (8 1/2" x 11") pages, excluding cover letter, one-page "Introduction" required when

submitting a revised (amended) application, Biographical Sketch (limited to 3 pages for each key person), letters of commitment from collaborators and consultants, "Checklist" (Form Page 5), "Personal Data on Principal Investigator" Form Page, and page(s) furnishing information required under "Prior SBIR/STTR Phase II Awards" (Section IV, item H), if applicable. The 25-page limit includes all other form pages and "continuation" pages suggested by these instructions or application form pages. Note: Sections A-D of the Research Plan are limited to a total of 15 pages.

2. Phase I appendices are not permitted and, if submitted, they will not be considered in the review of the application for scientific and technical merit.

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## B. TYPE SIZE

Type size specifications must be observed throughout the application or the application will be returned without review.
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The application must be clear, readily legible, and conform to the following requirements:

1. The height of the letters must not be smaller than 10 point.
2. Type density must be no more than 15 characters per inch (cpi). For proportional spacing, the average for any representative section of text must not exceed 15 cpi.
3. There must be no more than 6 lines of type within a vertical inch.
4. Margins must be at least ½ inch wide.
5. Figures, charts, tables, figure legends, and footnotes may be smaller in size but MUST be readily legible.

Type requirements should be checked on the printed document using a standard device for measuring type size, rather than relying on the font selected for a particular word processing/printer combination. The type size used throughout the application must conform to ALL of these requirements - applications not meeting these requirements will be returned without review.

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## C. FORM PAGE ENTITLED "PERSONAL DATA ON PRINCIPAL INVESTIGATOR"

As part of the design and implementation of Electronic Research Administration, the Public Health Service (PHS) is assessing measures for protecting private information, including the Social Security Number (SSN). Although the provision of the SSN is voluntary, it is critically important to the PHS for the accurate identification, referral, and review of applications and for efficient management of PHS grant programs. To provide the PHS with the information it needs for this important task, the SSN of the Principal Investigator should be provided at the top of the "Personal Data on Principal Investigator" form ONLY. The SSN should NOT be listed on the face page of the application, nor provided elsewhere in the application, for example, at the top of each application page.

In accordance with the instructions for completing the "Personal Data on Principal Investigator" form, attach it to the signed original of the application after the Checklist. Do not attach copies of this form to the duplicate copies of the application.

Upon receipt of the application by the PHS, this form will be separated from the application. This form will NOT be duplicated, and it will NOT be part of the review process. Data will be confidential and will be maintained in the Privacy Act record system 09-25-0036, "Grants: IMPAC (Grant/Contract Information)." A partially completed Personal Data Form Page is acceptable; that is, the proposed Principal Investigator may elect to provide some items but not all.

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## D. MARKET RESEARCH

The PHS will not support any market research under the SBIR/STTR programs. Neither will it support studies of the literature that will lead to a new or expanded statement of work. Literature searches where the commercial product is a database are acceptable.

For purposes of the SBIR/STTR programs, "market research" is the systematic gathering, editing, recording, computing, and analyzing of data about problems relating to the sale and distribution of the subject of the research project. It includes various types of research, such as

the size of potential market and potential sales volume, the identification of consumers most apt to purchase the products, and the advertising media most likely to stimulate their purchases. However, “market research” does not include activities under a research plan or protocol that require a survey of the public as part of the objective of the project to determine the impact of the subject of the research on the behavior of individuals.

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## E. PRIOR SBIR PHASE II AWARDS

A small business concern that submits an SBIR Phase I application and that has received more than 15 Phase II SBIR awards during the preceding five (5) fiscal years must document the extent to which it was able to secure Phase III funding to develop concepts resulting from previous Phase II SBIR awards. The following information must be submitted in the Phase I application regarding each such prior Phase II award: (1) name of awarding agency; (2) award number and date; (3) amount of award; (4) title of project; (5) source, date, and amount of Phase III funding agreement; and (6) commercialization status of each Phase II award shown in item 1 above.

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## F. ASSIGNMENT OF GRANT APPLICATIONS

The Center for Scientific Review (CSR) will assign appropriately completed applications to the Scientific Review Groups (commonly referred to as “SRGs” or “study sections”) that will perform the scientific/ technical merit review. In addition, CSR will assign each application to the agency awarding component that is the potential funding component.

**Cover Letters.** When submitting an application, the small business concern applicant organization may include a cover letter to suggest an awarding component(s) to which it could be appropriately assigned for potential funding, to indicate a specific area of expertise that should be represented on the study section, and to indicate a direct conflict of interest.

Identify competitors who have direct conflicts of interest. When the scientific areas and the research proposed in a grant application are sufficiently relevant to the program responsibilities of two or more awarding

components, CSR may assign the application to all such components. The component that has the most relevant program responsibility is designated as the primary assignee. The other components that have an interest in the application are designated as secondary assignees. If the application is eligible for funding and the primary assignee does not intend to make an award, the secondary assignees will be given the opportunity to do so. Although these suggestions will be taken into consideration, the final determination will be made by the agencies participating in this solicitation.

**Cover Letters:**

- Request assignment(s) to potential awarding components.
- Indicate requisite study section expertise.
- Identify competitors who have direct conflicts of interest.

## V. SUBMISSION OF SBIR/STTR GRANT APPLICATIONS

The NIH’s Center for Scientific Review (CSR) is the single receiving point for all NIH, CDC, and FDA SBIR/STTR grant applications.

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### A. RECEIPT DATES

**NOTE:** In CY 2001, SBIR and STTR applications have the same receipt dates.

Grant applications submitted under this SBIR/STTR Phase I Grant Solicitation must be received by the published receipt dates. *If the receipt date falls on a weekend, it will be extended to the following Monday; if the date falls on a holiday, it will be extended to the following workday.* An application received after the published receipt date may be acceptable if it carries a legible proof-of-mailing date assigned by the carrier and the proof-of-mailing date is not later than one week prior to the deadline date. The receipt date will be waived only in extenuating circumstances. To request a waiver, include an explanatory letter, addressed to the Division of Receipt and Referral, Center for Scientific Review, with the signed, completed application. No request for a waiver will be considered prior to receipt of the application, and there is no guarantee that the waiver will be granted.

## Receipt of SBIR/STTR Phase II Applications (non-"Fast-Track")

*Phase II applications may be submitted on any of the three scheduled receipt dates identified below, either before or after expiration of the Phase I budget period. However, Phase II grant applications should be submitted no later than the first six receipt dates following expiration of the Phase I budget period.*

Applicant small business concerns are reminded that Phase II funding is based on the results of Phase I, demonstration of feasibility, scientific and technical merit, and commercial potential of the Phase II application. Applicants are

cautioned that applications demonstrating insufficient results in Phase I may not receive a score in the peer review process (see Section VI, Method of Selection and Evaluation Criteria).

## Receipt of Fast Track Applications

Fast Track applications may be submitted on any of the three scheduled receipt dates below. The face pages for both the Phase I and Phase II portions should be clearly marked "Fast Track", and copies of both portions should be assembled and submitted together.

SBIR AND STTR RECEIPT DATES PHASE I AND PHASE II	NATIONAL TECHNICAL MERIT REVIEW	ADVISORY COUNCIL BOARD REVIEW	ESTIMATED AWARD DATE
April 1, 2001	June/July	Sept/Oct	November
August 1, 2001	Oct/Nov	Jan/Feb	March
December 1, 2001 *	Feb/March	May/June	July

*Applications to the Centers for Disease Control and Prevention may be submitted only on the August 1 and December 1 receipt dates.*

CDC and FDA do not participate in the STTR program.

## B. NUMBER OF COPIES

Original  
Plus 5 Copies

Submit the original and five exact, clear, single-sided photocopies of each application. The original must be signed by the Principal Investigator and a corporate official authorized to act for the applicant organization.

single-sided photocopies of the application in one package to:

Center for Scientific Review  
National Institutes of Health  
6701 Rockledge Drive  
Room 1040-MSC 7710  
Bethesda, MD 20892-7710  
Phone: (301) 435-0715

*Change zip code to 20817 for express mail  
or courier service.*

## C. BINDINGS AND PACKAGING

Do not bind or staple the six sets together, but secure each with rubber bands or paper clips. Do not include more than one set of applications in each mailing envelope.

## D. MAILING AND/OR DELIVERY ADDRESSES

Mail or deliver the complete, signed, and typewritten original and five signed, exact, clear,

## E. NOTIFICATION OF RECEIPT

Usually within six weeks after the receipt date, the CSR/NIH will send the Principal Investigator and the applicant organization a notification of receipt of the application. The mailer will indicate a grant application assignment number as well as the name, address, and telephone

number of the Scientific Review Administrator (SRA) of the Scientific Review Group (SRG) to which the application has been assigned. If this information is not received within that time, contact:

Division of Receipt and Referral  
Center for Scientific Review, NIH  
(301) 435-0715; Fax: (301) 480-1987

### Sample Grant Application Assignment Number

	SBIR Phase I Application	Serial Number	Amended Application
	↓	↓	↓
<b>1</b>	<b>R43</b>	<b>CA 12345</b>	<b>01 A1</b>
↑		↑	↑
New Application		Institute/Center	Grant Support Year

### F. INCOMPLETE APPLICATIONS

Do not submit an incomplete application. An application will be considered incomplete and will be returned if it is illegible, if it does not conform to the instructions, or if the material presented is insufficient to permit an adequate review.

### G. SUPPLEMENTARY OR CORRECTIVE INFORMATION

Supplementary or corrective material pertinent to the review of an application may be submitted after the receipt date, but only if it is specifically solicited by or agreed to through prior discussion with the Scientific Review Administrator of the SRG. In no instance can the original Phase I application plus supplementary materials exceed the Phase I Research Plan page limitations. In addition, the submission of CD-ROM disks as demonstration materials for Phase I SBIR/STTR applications is forbidden.

## VI. METHOD OF SELECTION AND EVALUATION CRITERIA

All Phase I and Phase II grant applications will be evaluated and judged on a competitive basis. Initially, applications will be screened for completeness and those found to be incomplete in any way or programmatically unrelated to the agency's mission will be returned without review

to the applicant small business concern. Those passing the initial screening will be reviewed for technical and scientific merit. Each application will be judged on its own merit, according to the review criteria described below. The participating agencies are under no obligation to fund any specific application or make any specific number of awards in a given research topic area. Also, they may elect to fund several or none of the proposed projects within a given topic area.

### A. REVIEW PROCESS

Grant applications are subjected to a peer review process involving two sequential steps that are required by law. The first step is performed by the Scientific Review Groups (SRGs), composed primarily of non-Federal scientists, physicians, and engineers (from academia and industry) selected for their expertise and stature in particular scientific fields. The second step is performed by the National Advisory Council or Board of the potential awarding component (Institute, Center, or other unit) to which the grant application is assigned.

### SCIENTIFIC REVIEW GROUPS

The first task of the SRGs is to evaluate each SBIR/STTR application for scientific and technical merit and potential for commercialization, and to make an SRG recommendation for each application on the basis of this evaluation. While NIH uses a numerical range from 1.00 (most meritorious) to 5.00 (least meritorious), a streamlined procedure is used to determine those applications that the SRG considers to be in the "upper" or "lower half". Applications in the "upper half" are discussed by the SRG and *generally* receive a score between 1.0 and 3.0, and applications in the "lower half" are not discussed and receive an "unscored" designation (i.e., those that would generally have received a score between 3.0 and 5.0). However, any review group member may identify an application that he or she believes should be discussed at the meeting and receive a numerical score. Under the currently employed streamlining procedures, a rating of 3.00 would be considered the median score for the cohort of applications that a scientific review group might review.

Individual reviewers mark scores to two significant figures, e.g., 1.2, and the individual scores are averaged and then multiplied by 100 to yield a single overall score for each scored application, e.g., 153. Abstaining members and those not present during the discussion do not assign a numerical rating and are not counted in calculating the average of the individual ratings.

The second task of the SRGs is to make budget recommendations concerning time and dollar amounts that are appropriate for the work proposed. The SBIR/STTR Phase I review criteria are listed in item C below.

Regardless of the study section recommendation, all applicants receive a summary statement that includes a single rating/designation and the essentially unedited, verbatim critiques of two or more assigned reviewers.

#### **NATIONAL ADVISORY COUNCIL OR BOARD**

The second level of review is performed by the National Advisory Council or Board of the potential awarding component (Institute, Center, or other unit) to which the grant application is assigned. These groups, composed of scientists, physicians, and members of the public, are chosen for their expertise, interest, or activity in matters related to the awarding component's mission. In order for an application to be funded, it must be recommended by the Council or Board.

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#### **B. RELEASE OF GRANT APPLICATION REVIEW INFORMATION**

Following evaluation of grant applications by the SRGs but prior to National Advisory Council or Board action, summary statements will be sent automatically to Principal Investigators.

Applicants normally receive their summary statement within four to six weeks following the study section meeting in which it was reviewed. A "summary statement" documents the evaluation of an application by the SRG and conveys the SRG's recommendations to the awarding component and its Council or Board. No one other than the Principal Investigator (and appropriate NIH staff) may receive the summary statement and evaluation rating.

After the review meeting occurs, applicants are encouraged to address inquiries about review to their Program Director, rather than to review staff. After receipt/review of the summary statement, applicants are encouraged to contact their Program Director for guidance and advice.

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#### **C. SBIR/STTR REVIEW CRITERIA**

"Formulae" do not exist for calculating an individual reviewer's score on an application. In considering the scientific and technical merit of each application, the following criteria will be used:

##### **1. *Significance***

- Does the proposed project have commercial potential to lead to a marketable product or process? Does this study address an important problem?
- What may be the anticipated commercial and societal benefits of the proposed activity?
- If the aims of the application are achieved, how will scientific knowledge be advanced?
- Does the proposal lead to enabling technologies (e.g., instrumentation, software) for further discoveries?
- Will the technology have a competitive advantage over existing/alternate technologies that can meet the market needs?

##### **2. *Approach***

- Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project?
- Is the proposed plan a sound approach for establishing technical and commercial feasibility?
- Does the applicant acknowledge potential problem areas and consider alternative strategies?
- Are the milestones and evaluation procedures appropriate?

### 3. ***Innovation***

- Does the project challenge existing paradigms or employ novel technologies, approaches or methodologies?
- Are the aims original and innovative?

### 4. ***Investigators***

- Is the Principal Investigator capable of coordinating and managing the proposed SBIR/STTR?
- Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers, including consultants and sub-awardees (if any)?

### 5. ***Environment***

- Is there sufficient access to resources (e.g., equipment, facilities)?
- Does the scientific and technological environment in which the work will be done contribute to the probability of success?
- Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements?

In accordance with NIH policy, all applications will also be reviewed with respect to the following:

- The adequacy of plans to include genders, minorities, and their subgroups, and children, as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.
- The adequacy of the proposed protection for humans, animals, or the environment to the extent they may be adversely affected by the project proposed in the application.
- The appropriateness of the proposed budget and its duration in relation to the proposed research.

## **Phase II Applications**

In addition to the above criteria, to what degree was progress toward the Phase I objectives met and feasibility demonstrated in providing a solid foundation for the proposed Phase II activity?

## **Phase I/Phase II Fast Track Applications**

For Phase I/Phase II Fast Track applications, the following additional criteria will be applied:

- Does the Phase I application specify clear, appropriate measurable goals (milestones) that should be achieved prior to initiating Phase II?
- Did the applicant submit a concise Product Development Plan that adequately addresses the four areas described in Section VI, item G of this solicitation?
- To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?
- Does the project carry a high degree of commercial potential, as described in the Product Development Plan?

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## **D. FUNDING DECISIONS**

When making funding decisions, the awarding components take into consideration the following: (1) ratings resulting from the scientific and technical evaluation process; (2) areas of high program relevance; (3) program balance (that is, balance among areas of research); (4) available funds; and (5) the commercialization status where the small business concern has received more than 15 Phase II awards in the prior five (5) fiscal years, if applicable (see this application requirement under “Prior SBIR Phase II Awards” found in the “Introduction and Application Instructions” portion of the solicitation). The awarding component will notify the Principal Investigator and the applicant small business concern of the final disposition of the application.

Fast-Track Phase II applications that are recommended for approval may be funded following submission of the Phase I progress

report and other documents necessary for continuation. Phase II applications will be selected for funding based on the project's scientific and technical merit, the awarding component's assessment of the Phase I progress report and determination that the Phase I goals were achieved, an update and verification of the Product Development Plan and any commitment(s) for funds and/or resources from an investor or partner organization, as described below, the project's potential for meeting the mission of the awarding component and for commercial success, and the availability of funds.

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## E. REVISION AND RESUBMISSION OF GRANT APPLICATIONS

Grant applications that are not funded may be revised for resubmission at a future receipt date. However, applicant organizations may submit no more than two revised (amended) applications within a time period of two years from the receipt date of the initial, original application. The limit of two revisions allows applicant small business concerns and Principal Investigators sufficient time to consider new findings in the area of research and to take a fresh start at their research plans.

Resubmitted applications without substantive changes will not be accepted. The revised application MUST address the issues identified in the previous summary statement for the previous submission that was not fund. Revised sections must be clearly marked (as described in the "Introduction and Application Instructions" portion of this solicitation). Upon acceptance of a revised application by the CSR, the prior version will be withdrawn from further consideration by the awarding components. Acceptance of the revised application will generally mean that it will fall into a later review and award cycle. Resubmission of an application that merely duplicates a previous application is not acceptable and the duplicate application will be returned without review.

### Amended (revised) Applications

For amended applications, in addition to the five review criteria described above, the following review criteria will be applied:

- Are the responses to comments from the previous Study Section adequate?

- Are the improvements in the revised application appropriate?

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## F. SUBMISSION OF SIMILAR GRANT APPLICATIONS BY THE APPLICANT ORGANIZATION

The submission of similar grant applications to the NIH by the same applicant small business concern is strongly discouraged. Principal Investigators are cautioned not to prepare multiple grant applications with essentially the same research focus, that is, a product or technology that, with non-substantive modifications, can be applied to a variety of purposes. In evaluating groupings of applications with a common scientific focus or objective (for example, implantation sensors/sensor materials, medical applications of lasers, immunology/immunoassays), SRGs are in a position to easily identify multiple grant applications from the same small business concern for essentially the same project. In these cases, the HHS will give funding consideration to only one application.

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## G. PHASE I/PHASE II FAST-TRACK REVIEW OPTION (Applicable to NIH Only)

The SBIR/STTR "Fast-Track" procedures described below are designed to expedite the decision and award of Phase II funding for scientifically meritorious applications for projects that have a high potential for commercialization. Fast-Track is a parallel review option available to those small business concerns (applicant organizations) whose applications satisfy additional criteria that enhance the probability of the project's commercial success. Applications that do not meet these criteria may be redirected for review through the standard review procedures described above.

Fast-Track offers two major advantages:

- Concurrent submission and peer review of both Phase I and Phase II projects.
- Minimal or no funding gap between Phase I and Phase II.

Fast-Track Phase II applications that are recommended for approval may be funded following submission of the Phase I progress report and other documents necessary for

continuation. Phase II applications will be selected for funding based on the project's scientific and technical merit, the awarding component's assessment of the Phase I progress report and determination that the Phase I goals were achieved, an update and verification of the Product Development Plan and any commitment(s) for funds and/or resources from an investor or partner organization, as described below, the project's potential for meeting the mission of the awarding component and for commercial success, and the availability of funds.

### **SBIR/STTR Fast-Track Application Instructions and Requirements**

- Complete Phase I and Phase II applications (including the Face page, Abstract, Budget, Biographical Sketch and Bibliography, and Research Plan) must be submitted in accordance with specific Phase I and Phase II grant application instructions and requirements. Incomplete Fast Track Applications will be returned without review.
- Identify the application as Fast-Track, by typing the words "Fast-Track" in Item 2 on the Face Page of the Phase I application. Also, type "fast-track" in **Item 1b** on the face page of the Phase II application.
- Prepare and submit both a Phase I and Phase II SBIR/STTR application together for concurrent initial peer review and evaluation. SBIR and STTR Phase I application forms and instructions are available electronically at <http://grants.nih.gov/grants/funding/sbirsttr/11instructions.htm>. SBIR Phase II application forms and instructions (<http://grants.nih.gov/grants/funding/sbir2/intro.htm>) as well as STTR Phase II application forms and instructions (<http://grants.nih.gov/grants/funding/sttr2/intro.html>) are also available electronically.
- A complete Phase I and Phase II application package must be mailed together in a single envelope or box.
- Review the **Fast Track Reminder Sheet** before submitting the application.

- Specify in the Phase I application clear, appropriate measurable goals (milestones) that should be achieved prior to initiating Phase II. Failure to provide clear, measurable goals may be sufficient reason for the scientific peer review group to exclude the Phase II application from Fast-Track review. The scientific peer review group will evaluate the goals and may suggest other milestones that should be achieved prior to Phase II funding.
- The Phase I and Phase II applications will receive a single rating. Following the initial peer review, Fast-Track applications will receive secondary review by the advisory council or board of the NIH awarding component that is the potential funding component.
- Submit a concise Product Development Plan (limited to ten pages). Label this section clearly and ***include it as part of the Research Plan (in lieu of the Phase I Final Report)***, after the Significance section and before the Experimental Design and Methods section of the Phase II application. Addressing each of the following areas:
  1. Company information: including size; specialization area(s); products with significant sales; and history of previous Federal and non-Federal funding, regulatory experience, and subsequent commercialization (see Section III of this solicitation for definition of "commercialization").
  2. Value of SBIR/STTR project, including lay description of key technology objectives, current competition, and advantages compared to competing products or services.
  3. Commercialization plans, milestones, target dates, market analyses of market size, and estimated market share after first year sales and after five years.
  4. Patent status or other protection of project intellectual property.

Applicants are ENCOURAGED to seek commitment(s) of funds and/or resources from an investor or partner organization for commercialization of the product(s) or service(s) resulting from the SBIR/STTR grant.

Before submitting applications under “Fast-Track,” applicant small business concerns and investigators are strongly encouraged to consult with the NIH program staff named in the table “Awarding Component/Agency Contact Information.”

## VII. CONSIDERATIONS

### A. AWARDS

The approximate number of Phase I grant awards to be issued under this solicitation are:

NIH	900 SBIR awards 100 STTR awards
CDC	15 awards
FDA	2 awards

The primary award mechanism will be the grant instrument. The average dollar amount of Phase I awards (composed of direct costs, indirect costs, and fixed fee) to be issued under this solicitation is estimated to be approximately \$100,000. The average dollar amount of Phase II awards (composed of direct costs, indirect costs, and fixed fee) to be issued to continue the research or R&D efforts initiated in Phase I, is estimated to be approximately \$750,000 for SBIR awards and \$500,000 for STTR awards.

### B. REPORTS

NIH requires that SBIR/STTR grantees submit the following reports within 90 days of the end of the grant support period unless an extension is granted by the Grants Management Office (GMO):

- Financial Status Report (OMB 269)
- Final Progress Report (no form)
- Final Invention Statement and Certification (HHS 568)
- Annual Invention Utilization Reports

Failure to submit timely final reports may affect future funding to the organization or awards with the same Principal Investigator.

### Final Financial Status Report (FSR) (OMB 269)

As stated in the *NIH Grants Policy Statement*, October 1998, Part II, pages 83-84, a Financial Status Report (OMB 269) must be submitted within 90 days of the expiration date. Reports of expenditures are required as documentation of the financial status of grants according to the official accounting records of the grantee Organization.

The FSR 269 form is available electronically at <http://www.whitehouse.gov/OMB/grants/index.html>. FSRs may be transmitted electronically to the NIH's Office of Financial Management (OFM), which, for this purpose, is equivalent to submission to the GMO. Information about the electronic transmittal of FSRs may be obtained from OFM at (301) 496-5287. Otherwise, the Financial Status Report may be mailed to:

Government Accounting Branch  
Office of Financial Management  
National Institutes of Health  
31 Center Drive, Room B1B05A, MSC 2050  
Bethesda, MD 20892-2050

Prior to submitting FSRs to NIH, grantees must ensure that the information submitted is accurate, complete, and consistent with the grantee's accounting system. The signature of the authorized institutional official on the FSR certifies that the information in the FSR is correct and complete and that all outlays and obligations are for the purposes set forth in grant documents, and represents a claim to the Federal Government. Filing a false claim may result in the imposition of civil or criminal penalties.

### Final Progress Report

**NOTE:** A Phase I Final Report is required for all Phase II applications. Specific instructions for submission of the Phase I Final Report are in the Phase II Grant Application kit.

However, if a Phase II application will not be submitted within 90 days of the Phase I project period end date, then submit one copy of the Phase I Final Report to the Grants Management Office of the Awarding Component within 90 days of the termination of the Phase I grant.

The Final Progress Report may be typed on plain white paper and should include, at a minimum:

- Beginning and end dates for the period covered by the SBIR/STTR Phase I grant.
- Key personnel who worked on the project during that period (include titles, dates of service, and number of hours devoted to the project).
- Summary of the specific aims of the Phase I grant.
- Succinct account of published and unpublished results, indicating progress toward achievement of the originally stated aims.
- List of titles and complete references to publications, manuscripts accepted for publication, patents, invention reports and other printed materials, if any, that resulted from the Phase I.

The recommended length for the narrative portion is 10 pages.

### Final Invention Statement and Certification

The grantee must submit to the awarding component a Final Invention Statement and Certification (HHS-568), whether or not an invention(s) results from work under the grant. The final invention statement/certification must be signed by the Principal Investigator and an authorized institutional official and must list all inventions that were conceived or first actually reduced to practice during the course of work under the project, from the original effective date of support through the date of expiration or termination, whether or not previously reported. If there were no inventions, the statement should indicate "None."

**IMPORTANT:** All inventions made in the course of, or under, any NIH research grant, including SBIR/STTR awards, must be promptly and fully disclosed to NIH within 2 months after the inventor provides written disclosure to the grantee's authorized official.

The disclosure must be in writing. Identify the applicable grant and the name of the inventor(s), and provide a complete technical description and other information as required by 37 CFR 401.14(c)(1) (see "Administrative Requirements

Availability of Research Results: Publications and Intellectual Property Rights, Including Unique Research Resources" for the full text of the clause).

In addition to immediate invention disclosure, each application for competing or non-competing continuation support of an NIH grant-supported research project must include either a listing of all inventions conceived or reduced to practice during the preceding budget period or a certification that no inventions were made during the applicable period.

### Annual Utilization Report

The grantee must also submit an annual utilization report when the grantee has elected title to an invention or when royalties or licensing fees are generated for inventions that are not patented. NIH has developed an optional online Extramural Invention Information Management System, known as "IEdition," to facilitate grantee compliance with the disclosure and reporting requirements of 37 CFR 401.14(h) (<http://www.iedison.gov>). Information from these reports is not made publicly available. For additional information on IEdition, see Section D below.

A summary of grantee/contractor invention responsibilities, which provides information on time limits placed by law and identifies specific invention reporting actions that must be taken, is provided at the end of this solicitation and is also available on the internet at <http://www.iedison.gov/timeline.html>.

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## C. PAYMENT SCHEDULE

Once an SBIR/STTR grant is awarded, the grantee will receive information and forms from the Payment Management System of the HHS regarding requests for cash, manners of payment, and associated reporting requirements. Payment may be made on a cost-reimbursement or advance basis.

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## D. LIMITED RIGHTS INFORMATION AND DATA

### Proprietary Information

Information contained in unfunded grant applications will remain the property of the

applicant. The Government may, however, retain copies of all applications. Public release of information in any application will be subject to existing statutory and regulatory requirements.

If proprietary information provided in an application constitutes trade secrets or proprietary commercial or financial information, confidential personal information or data affecting the national security, it will be treated in confidence, to the extent permitted by law, provided this information is clearly identified by the appropriate page numbers under the Notice of Proprietary Information on the Face Page of the SBIR/STTR grant application form. Any other notice may be unacceptable to the Government and may constitute grounds for return of the application without further consideration and without assuming any liability for inadvertent disclosure.

### **Title to Equipment and Supplies**

Title to equipment and supplies acquired by a for-profit organization as a grantee or subcontractor under a grant awarded by the agencies participating in this solicitation, shall vest, upon acquisition, in the grantee or subcontractor, respectively.

### **Rights to Data Developed Under SBIR/STTR Funding Agreement**

Rights to data, including software developed under the terms of any funding agreement resulting from a grant application submitted in response to this solicitation, shall remain with the grantee, except that the Government shall have the limited right to use such data for internal Government purposes and shall not release such data outside the Government without permission of the grantee for a period of four years from completion of the project from which the data were generated.

### **Copyrights**

The grantee may normally copyright and publish (consistent with appropriate national security considerations, if any) material developed with PHS support. The awarding component receives a royalty-free license for the Federal Government and requires that each publication contain an acknowledgment of agency support and disclaimer statement, as appropriate. An acknowledgment shall be to the effect that “This

*publication was made possible by grant number \_\_\_\_\_ from (NIH/CDC/FDA awarding component)” OR “The project described was supported by grant number \_\_\_\_\_ from (NIH/CDC/FDA awarding component). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the (NIH/CDC/FDA awarding component).”*

### **Inventions**

Any invention first conceived for reduced to practice with award funds must be reported to the NIH. The inventor must report the discovery to the grantee organization promptly. Within two months of the inventor's initial report to the grantee organization, the organization must report the invention to the NIH's Extramural Invention Reporting and Technology Resources Branch of the Office of Policy for Extramural Research (see address in “Patents” section below). This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 USC 202, and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

The reporting of inventions by the grantee organization to the NIH can be accomplished by submitting paper documentation, including fax, or electronically through the NIH Interagency Edison (IE Edison) Invention Reporting System. Use of the IE Edison system satisfies all mandated invention reporting requirements and access to the system is through a secure interactive Web site (<http://www.iedison.gov>) designed to ensure that all information submitted is confidential.

In addition to fulfilling reporting requirements, IE Edison notifies the user of future time-sensitive deadlines with enough lead-time to avoid the possibility of loss of patent rights due to administrative oversight. IE Edison can accommodate the invention reporting needs of all organizations. For additional information about this invention reporting and tracking system, visit the IE Edison home page cited above

or contact Edison via e-mail at [edison@od.nih.gov](mailto:edison@od.nih.gov).

## Patents

Small business concerns normally retain the principal worldwide patent rights to any invention developed with Government support. Under existing regulations, 37 CFR 401, the Government receives a royalty-free license for Federal Government use, reserves the right to require the patent-holder to license others in certain circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it substantially in the United States. The applicant small business concern is strongly encouraged to obtain information about additional requirements imposed by 37 CFR 401 from local counsel or from:

Extramural Invention Reporting and Technology Resources Branch  
Office of Policy for Extramural Research  
National Institutes of Health  
6701 Rockledge Drive, Room 3190, MSC 7750  
Bethesda, MD 20892-7750  
Phone: (301) 435-1986; Fax: (301) 480-0272  
Email: [gs60a@nih.gov](mailto:gs60a@nih.gov) or [edison@od.nih.gov](mailto:edison@od.nih.gov).

To the extent authorized by 35 U.S.C. 205, the Government will not make public any information disclosing a Government-supported invention for a four-year period from the date of disclosure to allow the grantee a reasonable time to file a patent application, nor will the Government release any information that is part of that patent application.

## Research Tools/Unique Research Resources

It is the policy of the NIH to make available to the public the results and accomplishments of the activities it funds. Restricted availability of unique research resources, upon which further studies are dependent, can impede the advancement of research and delivery of medical care. Notices in the *NIH Guide for Grants and Contracts* (Vol. 23, No. 26, July 15, 1994, <http://grants.nih.gov/grants/guide/1994/94.07.15/notice-public-health007.html>) and the *NIH Grants Policy Statement* ([http://grants.nih.gov/grants/policy/nihgps/part\\_ii\\_5.htm](http://grants.nih.gov/grants/policy/nihgps/part_ii_5.htm)) fully explain the policy regarding the distribution of research resources developed with NIH funds.

The NIH encourages the commercialization of research products and allows grantee organizations to make materials available to others for commercial purposes with appropriate restrictions and licensing terms. Where the product of research developed with Federal funding is a patentable but unpatented research product, the terms of a license must be no more restrictive than they would have been if the product had been patented.

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## E. PROFIT OR FEE

A reasonable fixed fee is available to small business concerns receiving awards under the SBIR/STTR program. The fee is not a “cost” item and may be used by the small business concern for any purpose, including additional effort under the SBIR/STTR award. The fee is intended to be a reasonable profit factor available to for-profit organizations, consistent with normal profit margins provided to profit-making firms for research and development work. However, the amount of the fee approved by the agencies participating in this solicitation normally will not exceed 7% of total costs (direct and indirect) for each phase (I and II) of the project. The fixed fee applies solely to the small business concern (grantee organization) receiving the SBIR/STTR award and not to any other participant in the project. However, the grantee may pay a profit/fee to a contractor providing routine goods or services in accordance with normal commercial practice.

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## F. JOINT VENTURES AND LIMITED PARTNERSHIPS

Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern in accordance with the definition in Section III.

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## G. AMERICAN-MADE EQUIPMENT AND PRODUCTS

When purchasing equipment or a product under the SBIR/STTR award, the small business concern should purchase only American-made items whenever possible.

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## H. TERMS AND CONDITIONS OF AWARD

Upon acceptance of a grant award, the grantee must comply with the terms and conditions contained or referenced in the Notice of Grant Award document. These terms and conditions, constituting legal requirements imposed on an awardee by statute, regulations, administrative policy, or the award document itself, are either “standard” or “special” as follows:

**Standard Terms and Conditions.** Those that are required by policy to be incorporated by reference in Notices of Grant Award through citations of specific documents that contain requirements applicable to the grant.

**Special Terms and Conditions.** Those that are judged necessary to attain the objectives for which the grant is being awarded, facilitate post-award administration, conserve grant funds, or otherwise protect the interests of the Federal Government. They are stated in full on the Notice of Grant Award.

Grant awards must be administered in accordance with the *NIH Grants Policy Statement* (<http://www.nih.gov/grants/policy/nihgps>) and with the following regulations and policy:

9 CFR 1,2,3	Animal Welfare
37 CFR 401	Rights to Inventions Made by Non-profit Organizations and Small Business Firms under Government Grants, Contracts, and Cooperative Agreements
42 CFR 52	Grants for Research Projects
45 CFR 46	Protection of Human Subjects
45 CFR 74	Administration of Grants
45 CFR 80	Nondiscrimination Under Programs Receiving Federal Assistance Through DHHS Effectuation of Title VI of the Civil Rights Act of 1964.
45 CFR 84	Nondiscrimination on the Basis of Handicap in Programs and Activities Receiving or Benefiting from Federal Financial Assistance

45 CFR 91	Nondiscrimination on the Basis of Age in Programs and Activities Receiving or Benefiting from Federal Financial Assistance
P.L. 99-158	Public Health Service Policy on Humane Care and Use of Laboratory Animals Section 495 “Animals in Research”
P.L. 100-690	Drug-Free Workplace Act of 1988 Title V, Subtitle D

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## I. ADDITIONAL INFORMATION

This Omnibus Solicitation is intended for informational purposes and reflects current planning. If there is any inconsistency between the information contained herein and the terms of any resulting SBIR/STTR funding agreement, the terms of the funding agreement are controlling.

Prior to award of an SBIR/STTR funding agreement, the Government may request the applicant small business concern to submit certain organizational, management, personnel, and financial information to ensure responsibility of the applicant organization.

This Omnibus Solicitation is not an offer by the Government and does not obligate the Government to make any specific number of awards. Awards under the SBIR/STTR program are contingent upon the scientific and technical merit and potential for commercialization of an application and the availability of funds for research and development. The Government is not responsible for any monies expended by the applicant organization before award of any funding agreement.

If an award is made pursuant to a grant application submitted in response to this Omnibus Solicitation, the grantee may be required to certify that it has not previously been, nor is currently being, paid for essentially equivalent work by any agency of the Federal Government. See Section III for the definition of “essentially equivalent work.” If an award is made under this Omnibus Solicitation for a project, some of whose elements are being or will be supported by another Federal agency, the awarding component and the applicant

organization will negotiate a budget that reflects the elimination of any overlapping support.

## VIII. SCIENTIFIC AND TECHNICAL INFORMATION SOURCES

Health science research literature is available at academic and health science libraries throughout the United States. Information retrieval services are available at these libraries and Regional Medical Libraries through a network supported by the National Library of Medicine. A list of Regional Medical Libraries and information about network services may be requested from the Public Information Office, National Library of Medicine, Bethesda, MD 20894, Phone: (301) 496-6308. Other sources that provide technology search and/or document services include the organizations listed below. They should be contacted directly for service and cost information.

### ***National Technical Information Service***

5285 Port Royal Road  
Springfield, VA 22161  
(703) 487-4600

### ***National Technology Transfer Center***

Wheeling Jesuit College  
316 Washington Avenue  
Wheeling, WV 26003-6295  
(800) 678-6882 (toll-free US)

### ***Mid-Atlantic Technology Applications Center***

University of Pittsburgh  
823 William Pitt Union  
Pittsburgh, PA 15260  
(800) 257-2725 (toll-free US)  
(412) 648-7003 (Fax)

### ***Mid-Continent Technology Transfer Center***

The Texas A&M University System  
College Station, TX 77843-3401  
(409) 845-8762  
(409) 845-3559 (Fax)

### ***Far West Regional Technology Transfer Center***

University of Southern California  
3716 South Hope Street, Suite 200  
Los Angeles, CA 90007-4344  
(800) 642-2872 (CA only)  
(800) 872-7477 (outside CA)  
(213) 746-9043 (Fax)

### ***Southern Technology Applications Center***

University of Florida  
College of Engineering, Box 24  
One Progress Boulevard  
Alachua, FL 32615  
(904) 462-3913  
(800) 225-0308 (outside FL)

### ***Center for Technology Commercialization***

Massachusetts Technology Park  
100 North Drive  
Westborough, MA 01581  
(508) 870-0042

### ***Great Lakes Industrial Technology Center***

25000 Great Northern Corporate Center  
Suite 260  
Cleveland, OH 44070-5310  
(216) 734-0094  
(216) 734-0686 (fax)

## IX. MODEL AGREEMENT FOR ALLOCATION OF RIGHTS

The STTR legislation (Public Law 102-564, as amended) and the STTR Policy Directive of the Small Business Administration (SBA), dated August 10, 1993, require that agencies participating in the STTR program provide guidance for allocating between small business concerns and research institutions intellectual property rights and rights, if any, to carry out follow-on research, development or commercialization. Included in this solicitation, is the guidance as approved by the SBA and the Office of the General Counsel, HHS. The document, entitled "[Model Agreement, Small Business Technology Transfer \(STTR\) Program, Allocation of Rights in Intellectual Property and Rights to Carry Out Follow-on Research, Development, or Commercialization](#)," may be photocopied freely. The parties to the Agreement are advised that this "model" may be revised through negotiation between the small business concern and the single, "partnering" research institution.

The Agreement is a requirement to receive support under the STTR program. Therefore, by signing the Face Page of the grant application, the Official Signing for Applicant Organization (small business concern) certifies that the Agreement with the research institution will be effective at the time of award. A copy of the Agreement must be furnished upon request of the NIH awarding component.

## X. GRANTS: PROGRAM DESCRIPTIONS AND RESEARCH TOPICS

The research topics shown in this solicitation represent program areas that may be of interest to applicant small business concerns in the development of projects that have potential for commercialization. Small business concerns are encouraged to submit SBIR/STTR grant applications in these areas.

However, SBIR and STTR (applicable to NIH only) grant applications will be accepted and considered in any area within the mission of the awarding components identified in this solicitation.

Applicants are encouraged to query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, and FDA awarding components. Additional information on each of the awarding components and their research interests is available electronically on the home pages indicated throughout this section of the solicitation.

The Fogarty International Center, which provides support only for conferences, postdoctoral fellowships for research in the United States and abroad, and senior scientist exchanges between the United States and other countries, does not participate in the SBIR/STTR program.

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### OFFICE OF PUBLIC HEALTH AND SCIENCE, OFFICE OF RESEARCH INTEGRITY (ORI)

ORI administers Public Health Service (PHS) research integrity activities on behalf of the Secretary of Health and Human Services (HHS) with the exception of the regulatory research integrity activities of the Food and Drug Administration. ORI facilitates a collaborative system for promoting integrity in biomedical and behavioral research supported or conducted by agencies of the U.S. Public Health Service (PHS). The system involves cooperative efforts among individual scientists, research institutions, and PHS agencies. For additional information about ORI visit <http://ori.hhs.gov>.

Development and dissemination of quality educational resources in the responsible conduct of research, for research professionals and trainees. Topics of interest include:

- A. **Data Acquisition, Management, Sharing, and Ownership.** Accepted practices for acquiring and maintaining research data. Proper methods for record keeping and electronic data collection and storage in scientific research. Includes defining what constitutes data; keeping data notebooks; data selection, retention, sharing, ownership, and analysis; data as legal documents and intellectual property, including copyright laws. Identification and understanding of existing federal and local policies relevant to the topic.
- B. **Mentor/trainee Relationships.** The responsibilities of mentors and trainees in pre-doctoral and postdoctoral research programs. Includes the role of a mentor, responsibilities of a mentor, conflicts between mentor and trainee, collaboration and competition, selection of a mentor, and abusing the mentor/trainee relationship. Identification and understanding of existing federal and local policies relevant to the topic.
- C. **Publication Practices and Responsible Authorship.** The purpose and importance of scientific publication, and the responsibilities of the authors. Includes topics such as collaborative work and assigning appropriate credit, acknowledgements, appropriate citations, repetitive publications, fragmentary publication, sufficient description of methods, corrections and retractions, conventions for deciding upon authors, authors' responsibilities, and the pressure to publish. Identification and understanding of existing federal and local policies relevant to the topic.
- D. **Peer Review.** The purpose of peer review in determining merit for research funding and publications. Includes topics such as, the definition of peer review, impartiality, how peer review works, editorial boards and ad hoc reviewers, responsibilities of the reviewers, privileged information and confidentiality. Identification and understanding of existing federal and local policies relevant to the topic.
- E. **Collaborative Science.** Research collaborations and issues that may arise from such collaborations. Includes topics such as setting ground rules early in the collaboration, avoiding authorship disputes, and the sharing of materials and

information with internal and external collaborating scientists. Identification and understanding of existing federal and local policies relevant to the topic.

- F. **Human Subjects.** Issues important in conducting research involving human subjects. Includes topics such as the definition of human subjects research, ethical principles for conducting human subjects research, informed consent, confidentiality and privacy of data and patient records, risks and benefits, preparation of a research protocol, institutional review boards, adherence to study protocol, proper conduct of the study, and gender, minority, and children's research issues. Identification and understanding of existing federal and local policies relevant to the topic.
- G. **Research Involving Animals.** Issues important to conducting research involving animals. Includes topics such as definition of research involving animals, ethical principles for conducting research on animals, federal regulations governing animal research, institutional animal care and use committees, and treatment of animals. Identification and understanding of existing federal and local policies relevant to the topic.
- H. **Research Misconduct.** The meaning of research misconduct and the regulations, policies, and guidelines that govern research misconduct in PHS-funded institutions. Includes topics such as fabrication, falsification, and plagiarism; error vs. intentional misconduct; institutional misconduct policies; identifying misconduct; procedures for reporting misconduct; protection of whistleblowers; and outcomes of investigations, including institutional and federal actions. Identification and understanding of existing federal and local policies relevant to the topic.
- I. **Conflict of Interest and Commitment.** The definition of conflicts of interest and how to handle conflicts of interest. Types of conflicts encountered by researchers and institutions. Includes topics such as conflicts associated with collaborators, publication, financial conflicts, obligations to other constituencies, and other types of conflicts. Identification and understanding

of existing federal and local policies relevant to the topic.

For additional information on research topics, contact:

Anita Ousley, Ph.D.  
Office of Research Integrity  
Phone: (301) 443-5300; Fax: (301) 443-5351  
Email: [aousley@osophs.dhhs.gov](mailto:aousley@osophs.dhhs.gov)

For administrative and business management questions, contact:

Ms. Kathleen Howe  
Grants Management Specialist  
National Institute of Neurological Disorder and Stroke  
6001 Executive Boulevard, Room 3266  
Bethesda, MD 20892  
(301) 496-7392; Fax: (301) 402-0219  
Email: [kh52x@nih.gov](mailto:kh52x@nih.gov)

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## NATIONAL INSTITUTES OF HEALTH (NIH)

The mission of the NIH is to improve human health through biomedical and behavioral research, research training, and communications. The programs of the NIH are oriented principally towards basic and applied scientific inquiry related to the causes, diagnosis, prevention, treatment, and rehabilitation of human diseases and disabilities; the fundamental biological processes of growth, development, and aging; and the biological effects of the environment. In addition, the NIH sponsors training of research personnel; career development of new and established scientists; evaluation and dissemination of new information about medicine and health; construction and renovation of research facilities and provision of other research resources; and improvements in biomedical communications.

To carry out these responsibilities, the NIH is organized into awarding components (Institutes/Centers). Those components that have an extramural element, that is, provide funds for research and research training activities in organizations external to the NIH, are shown below. The NIH makes every effort to finance worthy proposals, including the co-funding of such proposals by one or more awarding components having relevance in the projects.

## NATIONAL INSTITUTE ON AGING (NIA)

The NIA supports biomedical, behavioral, and social research and research training on the aging process as well as on the diseases and other special problems and needs of older people. It supports grant research under four established programs: Biology of Aging, Behavioral and Social Research, Neuroscience and Neuropsychology of Aging and Geriatrics.

Examples of research topics within the mission of the NIA that may be of interest to small businesses are shown below. These listings illustrate the range of areas that are of interest to the NIA and are not intended to be exhaustive.

For additional information about areas of interest to the NIA, please visit our home page at <http://www.nih.gov/nia>.

### Biology of Aging

Research on the physiology, molecular, and cellular basis of aging processes. NIA also has responsibility for maintaining existing resources and developing new resources for aging research, such as populations of well-characterized animals and specific cell lines, for example, human fetal lung fibroblasts. The Biology of Aging Program includes the following eight programmatic areas:

**ANIMAL MODELS.** The objective of the Animal Models Program is to identify and develop new animal models, both mammalian and lower organism, for use in aging research. This includes research on rats, mice, rabbits, non-human primates, insects, nematodes and yeast. Mutant and genetically-engineered rodent models of both normal aging and specific age-related pathologies are of particular interest.

Dr. Nancy Nadon  
(301) 496-0181, Fax: (301) 402-0010  
Email: [nn37a@nih.gov](mailto:nn37a@nih.gov)

#### A. *Systems Branch.*

**CARDIOVASCULAR BIOLOGY.** The objectives of the Cardiovascular Biology Program are to support basic research on age related changes in cardiovascular function, e.g. gene expression, and factors affecting cell death in heart tissue.

Dr. David Finkelstein  
(301) 496-6402, Fax: (301) 402-0010  
Email: [df18s@nih.gov](mailto:df18s@nih.gov)

**ENDOCRINOLOGY.** The purpose of the endocrinology of aging program is to support basic molecular and cellular research into the causes and effects of age-related changes in the endocrine system of humans and various animal models. Areas of investigation in this program include age-related changes in hormone production, metabolism, and action, diabetes, reproductive aging – male and female, biology of menopause, animal models of menopause, endocrine connections to menopause-related pathology in non endocrine systems, age-related changes in endocrine control of prostate growth, and endocrine aspects of age-dependent tumors.

Dr. Frank Bellino  
(301) 496-6402, Fax: (301) 402-0010  
Email: [fb12a@nih.gov](mailto:fb12a@nih.gov)

**IMMUNOLOGY.** Changes in the immune system of older people may contribute to the increased incidence of infection and cancer in the elderly. Research directed towards understanding the age-related regulation of immune function in health and disease is supported by BAP. Areas of investigation in this program include regulation of lymphocyte proliferation, regulation of immune specificity, response of immune system to biochemical stimuli, autoimmune disease and other immunopathology, endocrine and neuroendocrine control of immune function, molecular basis of the age-related decline in immune function, and interventions to retard and/or correct age-related decline in immune function.

Rebecca Fuldner  
(301) 496-6402, Fax: (301) 402-0010  
Email: [fuldnerr@mail.nih.gov](mailto:fuldnerr@mail.nih.gov)

**MUSCULOSKETAL BIOLOGY.** The age-related change of function of various physiologic systems often negatively impacts the health of the elderly. The purpose of this program is to support high quality basic molecular and cellular research to understand the causes and effects of these changes, thereby encouraging the development of

preventative and interventional strategies to extend the health span of the elderly. Areas of investigation in this program include age-related changes in osteoblast and osteoclast function and bone matrix, age-related changes in muscle structure and function, age-related changes in cartilage, connective tissue and skin, molecular mechanisms of the above age-related changes, and the molecular basis of osteoporosis and osteoarthritis.

Jill Carrington  
(301) 496-6402, Fax: (301) 402-0010  
Email: [jc189n@nih.gov](mailto:jc189n@nih.gov)

B. Genetics and Cell Biology Branch

**CELL STRUCTURE AND FUNCTION.** The objectives of the Cell Structure and Function Program are to support research on the molecular basis of age-related changes in signal transduction mechanisms, microenvironment – ECM, cell senescence/apoptosis/cancer, telomeres, and membranes and membrane receptors.

**GENETICS.** The objectives of the Genetics Program are to support research on identification and characterization of longevity assurance genes (LAGs) and senescence assurance genes (SAGs, genome stability, genomics, mouse mutagenesis; single nucleotide polymorphisms/genetic epidemiology, and Werner's syndrome.

Dr. Anna McCormick  
(301) 496-6402, Fax: (301) 402-0010  
Email: [am38k@nih.gov](mailto:am38k@nih.gov)

**METABOLIC REGULATION.** Areas of investigation in the Metabolic Regulation Program include nutrition/metabolism, age-related changes in mitochondrial function/mitochondrial dysfunction, mechanism of life span extension by caloric restriction, and generation of free radicals and oxidative stress.

Dr. David Finkelstein  
(301) 496-6402, Fax: (301) 402-0010  
Email: [df18s@nih.gov](mailto:df18s@nih.gov)

Areas that may be of interest to small businesses include, but are not limited to:

1. Effects of nutrition on the aging process, for example, the role of nutrition in determining longevity.

Dr. Pamela Starke-Reed  
(301) 496-6402, Fax: (301) 402-0010  
Email: [ps39p@nih.gov](mailto:ps39p@nih.gov)

2. Minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in young and old animals.
3. Instruments and/or methodology to monitor dynamic progression of ovarian follicles from primordial through antral stages in humans and other mammals with sufficient sensitivity to obtain an accurate profile during the perimenopausal period when relatively small numbers of follicles are present.
4. Development of appropriate animal and human culture model systems to explore underlying molecular and cellular mechanisms of prostate growth in middle-aged and older subjects.
5. Development of appropriate animal model systems to explore underlying molecular and cellular model systems of female reproductive aging processes as well as the development of pathophysiologic processes associated with the human menopause, including bone loss, cardiovascular pathology, hot flashes, and excessive uterine bleeding.

Dr. Frank Bellino  
(301) 496-6402, Fax: (301) 402-0010  
Email: [fb12a@nih.gov](mailto:fb12a@nih.gov)

6. Development of molecular probes such as antibodies, DNA sequences and expression vectors useful in studying aging, senescence, and longevity both in vivo and in vitro.
7. Mechanisms that control cellular proliferation and differentiation as well as differentiated cell models for aging research.
8. Mammalian genetic models to identify the genetic aspects of aging including studies intended to improve the nutrition and husbandry of such models

and the development of recombinant inbred strains.

Dr. Anna McCormick  
(301) 496-6402, Fax: (301) 402-0010  
Email: [am38k@nih.gov](mailto:am38k@nih.gov)

9. The development of antioxidant interventions to prevent oxidative damage in biological systems.
10. Development of interventions to slow down the degenerative processes associated with aging. These would include techniques with commercial potential to: (1) manipulate the control of cell proliferation or programmed cell death, (2) reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, (3) improve the damage surveillance and repair potential of cells, (4) improve the immune response to foreign molecules or reduce the response to self, and (5) reverse age-related changes in hormone production and function.

Dr. Huber Warner  
(301) 496-6402, Fax: (301) 402-0010  
Email: [hw7a@nih.gov](mailto:hw7a@nih.gov)

11. Development of animal models and transgenic animals for studying aging processes.
12. Development of new biological model systems for research on aging to replace or reduce vertebrate animal use in research. These models may include better in vitro systems, improved cell culture methods, mathematical models, and computer simulations.
13. Development of non-invasive research and test methods.
14. Development of biomarkers of aging in mammalian models of human aging.

Dr. Nancy Nadon  
(301) 496-0181, Fax: (301) 402-0010  
Email: [nn37a@nih.gov](mailto:nn37a@nih.gov)

15. Development of treatments for wound healing in the aged.

Dr. David Finkelstein  
(301) 496-6402, Fax: (301) 402-0010  
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## Behavioral and Social Research

Research on the psychological, social, cultural, demographic and economic factors that affect the process of growing old; the place of older people in society; unique problems facing the elderly; and the maintenance of health and effective functioning in the middle and later years. Special emphasis is placed on neglected groups of older people including, for example, oldest old, older minority populations, older women (including topics related to menopause), older adults living in rural areas, and older adults with developmental disabilities.

- A. *Individual Behavioral Process Branch.*  
Supports research and training on biopsychosocial processes linking health and behavior, cognitive functioning, human factors, and integrative approaches to the study of social, psychological, and physiological influences on health and well-being over the life course. Personality and social/interpersonal relationships are investigated as causal variables, and as mediators or moderators of the relationships between social/structural characteristics and health outcomes.

### BEHAVIORAL MEDICINE AND INTERVENTIONS.

Major research topics include: (1) disease recognition, coping and management, including physiological consequences of life stresses and burdens; and (2) social, behavioral and environmental interventions for health promotion, disease prevention, and disability postponement.

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**COGNITIVE AGING.** Supports research on changes in cognitive functioning over the life course. Studies are encouraged that: (1) examine the influence of contexts (behavioral, social, cultural, and technological) on the cognitive functioning and life performance of aging persons; (2) investigate the effects of age-related changes in cognition on activities of daily living, social relationships, and health status, and (3) develop strategies for improving everyday functioning through cognitive interventions. Major research topics include: higher-order cognitive processes (e.g., problem-solving, decision-making), social cognition, memory

strategies, perceptual skills, and reading and speech comprehension. Research is also welcomed that explores the role of individual difference factors in cognitive functioning (e.g., motivation, self-efficacy, beliefs about aging, emotions, sensory limitations, experience and expertise).

**PSYCHOLOGICAL DEVELOPMENT AND INTEGRATIVE SCIENCE.** Promotes research that applies an integrative approach to the study of health, behavior, stress and coping, and well-being over the life course. Studies are encouraged that combine diverse levels of analysis and examine reciprocal interactions among these levels. Examples include the effects of sociocultural, psychological (social, personality), biological, and genetic processes on behavioral and functional aging. In addition, research exploring factors at a single level that influence aging are welcomed.

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- B. *Population and Social Sciences Branch.* Supports research and training on the antecedents and impact of changing social, demographic, economic, and health characteristics of the older population. Research on the consequences of particular health care organizations and settings, and studies of the effects of other social institutions upon the health, well-being, and functioning of people in the middle and later years are supported. Comparative research is often appropriate, and interconnections with individual behavioral processes are encouraged.

**DEMOGRAPHY AND EPIDEMIOLOGY.** Embraces such topics as medical and biodemography; changes in the age-structure of populations, as well as studies on the prevalence and incidence of disease and disability, and age trajectories of health; life expectancy and active life expectancy; forecasting functioning, disability, morbidity, and mortality; migration and geographic concentrations of older people; rural-urban comparisons; distributions of health services and the long-term care system; race, ethnic, and socioeconomic variations; genetic epidemiology and population genetics.

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Ms. Angie Chon-Lee  
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**HEALTH AND RETIREMENT ECONOMICS.** Concentrates on the economics of aging, including but not limited to economic and health antecedents and consequences of work and retirement; pensions and savings; health insurance and health care expenditures; Medicaid, Medicare, and Social Security; interrelationships between health and economic status, including issues related to wealth, poverty, productivity, human capital development, and economic development; the economic costs of disability; cost-effectiveness of interventions; taxation policies on older people; cross-national comparisons.

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**HEALTH AND SOCIAL INSTITUTIONS.** Encourages research on the impact of a wide range of formal health care and related services, with particular emphasis on long-term care systems and settings and on the health and well-being of older persons. It also examines how social institutions (e.g., work, family, religion, community, living arrangements influence health outcomes in the later years and the ways in which people influence and are influenced by the network of cultural and social institutions surrounding them.

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Areas that may be of interest to small businesses include, but are not limited to:

1. Cognitive and human factors interventions on the individual and environment to maintain independence, maintain functioning, increase well being, and prevent disease/disability. Such interventions can include

behavioral technologies, environmental modifications and redesign, training and teaching efforts, or new programs, products and services. Interventions can be developed for home, community, health-care or work-place settings.

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2. Social, behavioral, environmental and/or technical interventions on the individual for health maintenance and disease/disability prevention. Such interventions can include self care assessments and behavioral change technologies, enhancing older patient-doctor interactions, environmental modifications and redesign, training efforts, or new programs, products and services to increase the health, functioning and well-being of older people. Interventions can be developed for home, community, health-care or work place settings.
3. AIDS and aging. Development of intervention strategies to prevent the spread of AIDS in middle-aged and older populations. Health education programs to inform the health care providers and public about risks of AIDS in older people.

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4. Interventions on the health-care system. Development and evaluation of strategies to improve health-care organization and delivery including attention to evolving structures for delivering care such as managed care, assisted living, subacute units in hospitals and nursing homes, and new forms of in-home care.
5. Interventions for care provision. Development of strategies for care providers (both professionals and families) to deal with burdens of care associated with chronic disabling illness or disease (including Alzheimer's disease). Interventions include new forms of adult day care, special care units and family

interventions. Development of work site programs to supply information on caregiving (including community respite and daycare facilities) and to enable advance planning by employees.

6. Elder abuse. Programs and interventions to prevent or reduce elder abuse and neglect in family or community settings and to reduce the susceptibility of older people to crimes, exploitation and victimization.
7. Death and dying. Programs that deal with decreasing the trauma and difficulty of elders, their families, and care providers in end-of-life decisions and those events that surround the end of life.

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8. Forecasting. Development of mathematical, economic, demographic and epidemiological models that will lead to improved forecasting of national, state and county level estimates of demand for aging-related services and improved prediction of the effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. For example, micro- and macro-simulation models of changes in health and economic status and methodological enhancements to existing models that take into account health, intergenerational transfers, changes in family composition, and other characteristics of future cohorts.
9. Measurement instruments and database support.
  - a. Development of new instruments using existing demographic and economic data and theory that yield defensible estimates of quality of health plans, hospitals, nursing homes, etc.
  - b. Development of improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research.

- c. Development of computer-assisted personal and telephone instrument modules, including expert systems, to use with older respondents, in order to determine occupational status, migration, housing issues, disability status, and family structure.
  - d. Development of new databases (e.g., from administrative data) and database support to satisfy data and research needs on aging, and innovative data archives and methods for accessing archives to make current statistical and epidemiological data more accessible to researchers.
  - e. Development of innovative methods and software to provide improved high performance remote analytic access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality and the need to prevent re-identification of subjects or respondents. Such software would increase the ease with which data analysts could perform sophisticated analyses with a wide range of statistical software programs, while automatically preventing any analyses or remote requests that could compromise data security.
10. Dissemination and teaching materials. Development of innovative teaching and dissemination tools (e.g., dataset-based computer programs, simulations/games, videotapes and other heuristic devices) to teach dynamics of population aging and convey results of aging research. For example, teaching modules for secondary students using US Census Bureau historical and projection data.

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## Neuroscience and Neuropsychology of Aging

Research on age-related changes in the brain or nervous system in the context of other age-related physiological or homeostatic regulator changes (e.g., endocrine, dietary, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, perceptual and cognitive processes and changes that occur with aging as related to their underlying biological mechanisms. An important component of this program is the support of studies on Alzheimer's disease and related dementias of aging. Areas that may be of interest to small businesses include, but are not limited to:

- A. Devices or intervention strategies that may prolong independence when there are dysfunctions of the central nervous system.
  - B. The development of sensitive, specific and standardized tests for diagnostic screening of cognitive decline and dementia, for example, the development of biochemical and neuroimaging criteria for the diagnosis of cognitive decline and Alzheimer's disease.
  - C. Discovery, development and/or evaluation of drugs, delivery systems, or treatments to enhance cognitive functioning in normal aging and to treat the cognitive deterioration and/or behavioral symptoms associated with Alzheimer's disease as well as to slow and/or reverse the course of the disease, or prevent it entirely.
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- D. Nutritional interventions to restore brain biochemical changes in aging and neurodegenerative diseases.
  - E. Biosensors and prosthetic devices to aid sensory and memory dysfunctions.
- Dr. Judith Finkelstein  
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- F. New technologies to screen for the presence of sleep disorders in older persons, to aid in the diagnosis of these disorders, and to enable their remediation.

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- G. Improved instrumentation, imaging technology, related devices, and software packages for use in visualizing neural activity during cognitive or sensory behavior in older adults. Also of interest would be new technologies to combine neural imaging and behavioral assessment in awake unanesthetized animals.

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- H. Development of technology and analysis tools to examine cellular patterns of gene and protein expression in the normal and diseased aging nervous system, including the identification of aberrant gene products expressed in the aging brain. Development of molecular imaging technology for the in vitro and in vivo analysis of gene and protein function in the aging brain.

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## Geriatrics

The Geriatrics Program supports research on prevention, treatment, and diagnosis of clinical problems that occur predominantly among older persons or that are associated with increased morbidity and mortality in older people; investigations of clinical problems associated with nursing homes and other sites of long-term care for frail older persons. Areas of interest include but are not limited to:

- A. Research on better ways to prevent injuries and deaths associated with the use of currently available bed rails in older patients; this will include improved designs of bed systems for use in the home, nursing home and hospital.
- B. Development of registries and databases on long-lived healthy pairs of relatives or members of families, suitable for use in genetic epidemiologic studies of aging.
- C. Development of devices and techniques for screening substantial numbers of individuals for particular alleles at loci of

relevance to human genetic studies of aging.

- D. Development of vaccines and other agents for preventing and treating infections in older persons, including development of new vaccines or preventive interventions, and new methods using currently available vaccines or preventive medications.

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- E. Refinements in techniques for the measurement of age-related changes in hormone levels, status or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function). The objective is to enhance sensitivity and achieve greater economy in the assay cost.

- F. Effects of menopause on woman's aging and subsequent health. Effects of age-related changes in endocrine status in men on subsequent aging, morbidity and mortality.

1. Refinements in techniques for the measurement of age-related changes in hormone levels or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function).
2. Development and testing of alternative strategies (to conventional estrogen/progestin therapy) for the management of short-term menopausal symptoms and for the reduction in risks of cardiovascular disease, osteoporosis, and other menopause-related conditions, disorders and diseases. Development and testing of new tissue-specific modulators of estrogen/androgen receptor activity in men and in women for the prevention or treatment of age-related diseases.
3. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases

- (e.g., osteoporosis) or (2) to predict or monitor efficacy of treatment or enhanced risk or progression of adverse effects/events.
4. Determine drug interactions, i.e., potential alterations in pharmacokinetics and pharmacodynamic properties of drugs taken concomitantly with postmenopausal hormones.
- G. Osteoporosis. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy, response to treatment or enhanced risk or progression of adverse effects/events.
- Dr. Sherry Sherman, Ph.D.  
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- H. Techniques for preventing or treating urinary incontinence.
- I. Improved instrumentation (e.g., accelerometers) for assessment of physical activity, and improved monitors for visually and/or biomechanically characterizing falls in older patients.
- J. Improved instrumentation and imaging techniques for measuring body composition and properties such as muscle function in older persons.
- K. Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).
- L. Measurement of deficits in muscle strength and balance among older persons.
1. Instrumentation for biomechanical assessment of ambulation and falls.
  2. Quantitative methods of assessing postural perturbations relevant to activities of daily living.

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- M. Techniques and methods for screening, diagnosis, and treatment of cancer in older persons.
1. Development of geriatric assessment instruments and/or methodology to assist oncologists in patient evaluation and diagnostic work-up to determine the older patient's overall physical and physiologic health status.
  2. Techniques to promote effective pain management in older-aged cancer patients. This includes documentation and assessment of pain intensity and its characteristics prior to and after pharmacologic and nonpharmacologic interventions.
  3. Development of innovative teaching tools for physicians, nurses, and other health professionals in the following areas: (1) to convey benefits of screening and early detection of cancer for use with older-aged persons; (2) to assist in teaching older-aged patients in self-examination for early warning signs of cancer; and (3) to teach older aged patients how to care for themselves after cancer surgery (e.g., ostomy patients).
  4. Development of methods to be used as guidance for physicians to estimate proper medication dosage in elderly cancer patients given body composition, size, age, other health problems, kidney functioning, and other physiologic parameters. This includes estimates of an initial or loading dose of therapeutic drugs and daily maintenance for continuance of therapeutic concentration of drugs in the patient's bloodstream.

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#### **Other Research Topic(s) Within Mission of Institute**

For additional information on research topics, contact:

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Bethesda, MD 20892-9205  
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For administrative and business management questions, contact:

Ms. S. Linda Whipp  
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National Institute on Aging  
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### **NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)**

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. The NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

For additional information about areas of interest to the NIAAA, please visit our home page at <http://www.niaaa.nih.gov/>.

### **Pharmaceutical Development for Alcoholism Treatment**

Applied and, where appropriate, clinical research on pharmacologic agents for use in the treatment or medical management of alcoholism, disorders resulting from alcoholism, the improvement and refinement of drugs currently available for therapeutic purposes, or drugs suitable for use in basic research studies on alcohol addiction. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of agents to attenuate drinking behavior, e.g., drugs to curb craving.

- B. Development of aversive agents such as disulfiram that attenuates drinking behavior.
- C. Development of agents to treat acute alcohol withdrawal.
- D. Development of agents to treat the protracted withdrawal syndrome.
- E. Development of neurotransmitter agonists and antagonists, or drugs that enhance the efficacy of neurotransmission, which are capable of improving or reversing alcohol-induced cognitive impairments.
- F. Development of agents to induce sobriety in intoxicated individuals (amethystic agents).
- G. Development of agents to diminish drinking by treating associated psychiatric disorders and/or drug abuse.
- H. Development of improved methods of drug delivery for the treatment of alcoholism. The systems developed must be capable of maintaining therapeutic drug levels for extended periods of time to alleviate compliance problems.
- I. Development of drugs for the treatment of alcoholic hepatitis and cirrhosis.
- J. Research on the pharmacokinetics of concurrent ethanol and other drug use.

For clinical questions, contact:

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For pre-clinical questions, contact:

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### **Diagnostic Assessment of Alcohol Use Disorders and Comorbidity**

Innovative self-report and biochemical approaches to the early identification of alcohol use problems and diagnosis of alcohol use disorders and comorbidity are needed. The research design should include measurements of reliability and validity in appropriate population samples. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development or adaptation of diagnostic instruments measuring alcohol use disorders and related comorbid conditions

in general population and treated samples, including youth, the elderly, pregnant women, ethnic minorities, the handicapped, and persons with low-level reading skills).

- B. Development and testing of methodology to translate diagnostic instruments for alcohol use disorders and associated disabilities into relevant different languages (e.g., various Hispanic languages).
- C. Development and testing of computer algorithms necessary to derive diagnoses of alcohol use disorders and associated comorbidity.
- D. Development of computer software for utilization of assessment instruments in a clinical setting. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.
- E. Application of statistical and mathematical analyses to develop models designed to increase our understanding of (1) etiologic relationship between alcohol use disorders and their associated disabilities, and (2) the factors that influence the initiation and maintenance of alcohol use disorders.
- F. Identification, validation, and assay of physiological and/or biochemical measures capable of identifying individuals at risk for becoming alcoholics or individuals who already exhibit alcohol problems. The accurate measurement of acetaldehyde conjugates or abnormal glycoconjugates in blood is one promising approach.
- G. Development of biochemical/physiological methods for early detection of alcohol-derived pathology, e.g., alcoholic hepatitis or cirrhosis. Development and characterization of markers to accurately predict vulnerability to alcohol-derived pathology.

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### **Treatment of Alcoholism**

Development and evaluation of innovative treatment approaches. Development and validation of tools to aid in the clinical management of patients. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development and evaluation of innovative treatment approaches. These approaches can include outreach, shelter, detoxification, treatment and recovery, and alcohol-free housing, as appropriate.
- B. Development and validation of tools to aid in the clinical management of patients, including selection of appropriate interventions, process evaluation, assessment of outcome, aftercare, and patient tracking, in various treatment settings.

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### **Measurement of Alcohol Consumption/Impairment**

Development of new methods for quantitative measurement of alcohol consumption, development of new and more accurate cost-effective technological approaches for non-invasive measurement of blood alcohol concentration, and development of novel approaches to measure and quantify alcohol-induced impairment of human performance. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of new methods for quantitatively estimating alcohol use over a period of days or weeks. The approaches should have high sensitivity and specificity and have utility in a variety of settings, including treatment compliance monitoring. Integration of measurement devices with electronic devices to transmit and/or record data in real time is desirable.
- B. Development of new and more accurate cost-effective technological approaches (such as breathalyzers) for non-invasive measurement of blood alcohol concentration in law enforcement, workplace, research, and clinical settings.
- C. Development of instruments involving tests of behavioral, cognitive, and/or motor function to measure and quantify alcohol-induced impairment of human performance. Such instruments may be computer-based and may be designed to simulate specific work situations such as driving performance, use of complex machinery, learning and retention of new information.

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## Prevention

Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Applicants are strongly encouraged to consult with research methodologists and statisticians to ensure that state-of-the-art approaches to design, analysis, and interpretation of studies under this topic are used. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Special emphasis should be placed on the needs of high risk groups, ethnic and minority populations, youth, children of alcoholics, women, the handicapped, and the elderly. Examples of such materials include school-based curricula, interactive videos, computer-based multimedia programs, training manuals for teachers or parents, and community-based programs.
- B. Development and evaluation of educational materials designed to inform the elderly about specific age-related risks for alcohol problems. Particular attention should be given to age-related reductions in alcohol tolerance, interactions between alcohol and prescription and over-the-counter medications, possible exacerbation of some medical conditions common among the elderly, potential biomedical and behavioral consequences of excessive alcohol use, and the role of alcohol in falls, fires, burns, pedestrian and traffic injuries, and other accidents.
- C. Development and evaluation of educational materials designed to provide information on date rape, spouse abuse, child abuse, and other types of violence that have been found to be associated with alcohol use and/or abuse. The development of

strategies for preventing victimization would also be appropriate.

- D. Development of instruments and educational materials designed to improve the effectiveness of employee assistance programs, especially with respect to assessment, referral, and health promotion as it relates to alcohol use and abuse.
- E. Development and evaluation of statistical analysis programs tailored to the design and analysis of alcohol prevention-relevant research. Programs could focus on a variety of areas including: imputation of missing data under varying design assumptions; simulation of distributions of outcomes based on varying mixtures of sample populations; application of chronic or infectious disease models to targeted communities; and models of the potential effect of various policy-based interventions, such as increased taxation or reduction of outlet density by license revocation and control.

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## Training in Alcoholism Assessment and Treatment Techniques

Development of educational materials, including computer-based approaches, for training of health professionals in the use of various assessment techniques and treatment strategies. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of educational materials, including computer-based approaches, for training of health professionals and paraprofessionals in the use of various assessment techniques and instruments.
- B. Development and evaluation of clinical protocols which enable health professionals to relate assessment to appropriate intervention and treatment strategies.
- C. Development and evaluation of effective health professions training programs which utilize state-of-the-art educational technology and are based upon currently accepted clinical and behavioral strategies. Examples include experiential teaching technologies such as standardized patient, interactive video, and computer simulation.

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### **Fetal Alcohol Syndrome (FAS) and Alcohol-Related Birth Defects**

FAS is a severe developmental disorder that includes mental retardation, cognitive and behavioral disabilities, and motor impairment. The NIAAA supports research leading to improved diagnosis and assessment of impairment and disability, as well as the development of tools to enhance academic and daily living skills. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of diagnostic and/or screening methods that can be used prenatally to identify fetuses affected by ethanol.
- B. Development and validation of assessment methods to provide more accurate clinical diagnosis of FAS at all life stages.
- C. Development and testing of skill-building, therapeutic, and education program products that enhance the social, cognitive, adaptive and motor abilities of individuals with FAS or fetal alcohol effects.
- D. Development of accurate measures of the responsiveness of children affected by prenatal exposure to alcohol to stress and predictors of vulnerability to alcohol-drinking or other psychopathology during adolescence and adulthood.
- E. Development and evaluation of educational and training programs designed to enhance the skills of non-professional caregivers and educators in dealing with the problems associated with FAS.

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For basic research questions, contact:  
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### **Science Education**

The NIAAA Science Education program is intended to: (1) supplement in-service education of health professionals and paraprofessionals with respect to their recognition and treatment of alcohol-related medical problems; (2) stimulate the interest of both precollege and college students, especially among underserved populations, in career opportunities in the biomedical and behavioral sciences generally and the alcohol field specifically; (3) enhance precollege education in the classroom, both directly and via support to teachers, in the life sciences and in education regarding science-related personal and societal challenges; and (4) improve public understanding of science generally and with particular regard to the role of and need for alcohol research. The NIAAA Science Education program complements, but does not duplicate, the education and training components described under other NIAAA topics.

Efforts in science education might include, but are not limited to:

- A. The development of methodology to transfer new alcohol research knowledge and directions of scientific knowledge growth to curriculum developers and science teachers, consistent with the National Research Council's National Science Education Standards (1996).
- B. The development and testing of specific science education materials, activities or programs to implement one (or more) of the four stated objectives of the NIAAA science education program. The creative use of emerging educational and telecommunications technologies in this regard is of special interest.
- C. The development and testing of methodology to present science and alcohol abuse-related curricula and educational materials to particular underserved group(s) in culturally relevant ways, and/or to obtain community support for education in science-related and alcohol-related topics that may be culturally sensitive.
- D. The development of resource materials on scientific career opportunities in fields of interest to NIAAA, reflecting activities (e.g. focus groups) and research on motivational factors influencing high school students'

career choices, and reflecting economic and social projections of career outlooks for the 21st century.

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### Research Tools

The NIAAA supports basic and applied research to develop new or improved tools to enhance laboratory studies on humans and animals. Examples include transgenic animal models, cell lines, new ligands for neuroimaging, and simulators of alcohol impairment. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of animal models, including transgenic animals, possessing specific traits of significance for the study of alcoholism, or for the study of specific pathologic disease states which arise from excessive alcohol consumption.
- B. Development of a hepatocyte cell line capable of maintaining viability and metabolic functions in culture systems for an indefinite period.
- C. Development of new methods of ethanol administration to animals that produce precise dose control.
- D. Development of specialized cell culture chambers to provide controlled administration of ethanol to in vitro cell systems.
- E. Development of ligands for alcohol-relevant neurotransmitter systems which will enhance the potential usefulness of PET and SPECT imaging technologies for the study of the etiology of alcoholism and related brain pathology.
- F. Development of instruments that simulate driving, piloting aircraft, or using other complex machinery under hypothetical or actual drinking handicaps and are designed to predict fatal and nonfatal accident involvement.

Laurie Foudin, Ph.D.  
(301) 443-0912  
Email: [lf29z@nih.gov](mailto:lf29z@nih.gov)

### Other Research Topic(s) Within Mission of Institute

For additional information on research topics, contact:

Dr. Michael Eckardt  
National Institute on Alcohol Abuse and Alcoholism  
(301) 443-6107; Fax: (301) 443-6077  
Email: [me25t@nih.gov](mailto:me25t@nih.gov)

For administrative and business management questions, contact:

Ms. Linda Hilley  
Grants Management Officer  
National Institute on Alcohol Abuse and Alcoholism  
(301) 443-4704; Fax: (301) 443-3891  
Email: [lh67b@nih.gov](mailto:lh67b@nih.gov)

### NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

The NIAID's Division of AIDS, Division of Allergy, Immunology, and Transplantation, and Division of Microbiology and Infectious Diseases fund SBIR/STTR grants on topics related to their mission and activities as described below. Questions on specific research areas may be addressed to the NIAID Branch Chiefs listed below. General questions on the NIAID SBIR programs and on administrative and business management may be addressed to contacts listed at the end of the NIAID section. When possible, applicants are encouraged to use email for communication.

For additional information about areas of interest to the NIAID, please visit our home page at <http://www.niaid.nih.gov>.

### Division of AIDS

The Division of AIDS (DAIDS) supports research on the pathogenesis, natural history, and transmission of HIV and HIV disease, and promotes progress in its detection, treatment, and prevention.

Director: Dr. Jack Killen  
(301) 496-0545  
Email: [jk31e@nih.gov](mailto:jk31e@nih.gov)

## BIostatistic Research Branch

Statistical methods in HIV studies.

Chief, Dr. Dennis O. Dixon  
(301) 402-2306  
Email: [dd23a@nih.gov](mailto:dd23a@nih.gov)

## BASIC SCIENCES PROGRAM

Supports basic and applied research on the causes, diagnosis, and prevention of HIV and AIDS.

Dr. Carl Dieffenbach  
(301) 496-0637  
Email: [wd6u@nih.gov](mailto:wd6u@nih.gov)

- A. *Epidemiology Branch*. Population-based research of HIV transmission and associated biological, behavioral, and environmental factors including correlation between immunologic and virologic events and clinical outcome trends in natural history; correlation between immunologic and virologic events and clinical outcome; and trends in natural history.

Chief: Dr. Paolo Miotti  
(301) 496-9176  
Email: [pm122m@nih.gov](mailto:pm122m@nih.gov)

- B. *Pathogenesis Branch*. Molecular and cellular biology, virology, and immunology of virus-host interactions and mechanisms of immunopathogenesis and HIV transmission.

Chief: Dr. Susan Plaeger  
(301) 402-9444  
Email: [sp218p@nih.gov](mailto:sp218p@nih.gov)

- C. *Targeted Interventions Branch*. Research areas: (1) targeted therapeutics emphasizing under-explored viral and cellular targets; (2) innovative therapeutic strategies including immune-based and gene-based therapies and therapeutic vaccines; (3) translational research for effective therapeutics spanning preclinical discovery to pilot clinical studies in humans; (4) preclinical discovery and development of topical microbicides and other entities for non-vaccine prevention strategies; and (5) animal models for evaluating new therapeutic entities, regimens, and strategies.

Chief: Dr. Nava Sarver  
(301) 496-2970  
Email: [ns18p@nih.gov](mailto:ns18p@nih.gov)

## VACCINE AND PREVENTION RESEARCH PROGRAM

Supports the development of vaccines and other biomedical and behavioral interventions to prevent AIDS.

Associate Director: Dr. Margaret (Peggy) Johnston  
(301) 402-0846  
Email: [pj7p@nih.gov](mailto:pj7p@nih.gov)

- A. *Vaccine Clinical Development Branch*. Research areas: (1) coordination of phase I, II, and III domestic and international clinical trials of candidate AIDS vaccines; (2) coordination of the characterization of immune responses in HIV-infected and uninfected immunized volunteers; and (3) coordination of studies to identify, validate, and standardize immunologic and virologic markers for monitoring response of participants in vaccine clinical trials.

Chief: Dr. Jorge Flores  
(301) 496-8200  
Email: [jf30t@nih.gov](mailto:jf30t@nih.gov)

- B. *Prevention Science Branch*. Coordination and support of epidemiologic and behavioral research on adolescents and adults, and to prevent HIV transmission; and coordination of domestic and international phase I, II, and III clinical trials to evaluate HIV/AIDS prevention strategies, including microbicides, chemoprophylactic agents, and other biomedical and behavioral risk reduction interventions.

Chief: Dr. Rodney Hoff (acting)  
(301) 496-6177  
Email: [rh25v@nih.gov](mailto:rh25v@nih.gov)

- C. *Preclinical Research and Development Branch*. Support of applied preclinical development of candidate AIDS vaccines, delivery methods, and adjuvants for the prevention of AIDS; promotion and evaluation of safety and efficacy of the prevention modalities, especially novel vaccine concepts identified in preclinical models including trials in non-human primates; genetic and immunologic variation; and mucosal immunity in SIV, HIV, and SHIV models.

Chief: Dr. James Bradac  
(301) 435-3754  
Email: [jb68k@nih.gov](mailto:jb68k@nih.gov)

- D. *Vaccine Research Branch*. Support of multidisciplinary research on mechanisms of immunity and pathobiology of HIV and related lentiviruses; and use of information obtained on the mechanism of viral and immune pathogenesis of HIV disease to design and promote novel vaccine strategies for HIV prevention.

Chief: Dr. Carl Dieffenbach (acting)  
(301) 496-0637  
Email: [cd17u@nih.gov](mailto:cd17u@nih.gov)

#### **THERAPEUTICS RESEARCH PROGRAM**

Develops and oversees research and development of therapies for HIV disease, including opportunistic infections (OI) and cancers, in adults, infants, children, and adolescents.

Associate Director, Dr. William Duncan  
(301) 496-8210  
Email: [wd6u@nih.gov](mailto:wd6u@nih.gov)

- A. *Clinical Research Management Branch*. Management of grants and contracts supporting therapeutic clinical trials.

Chief: Dr. Fred Batzold  
(301) 402-0143  
Email: [fb10c@nih.gov](mailto:fb10c@nih.gov)

- B. *Drug Development and Clinical Sciences Branch*. Preclinical development of experimental therapies; maintenance of a database of potential anti-HIV and -OI compounds; immunologic, virologic, and pharmacologic research related to the design and conduct of clinical trials.

Chief: Dr. Jonathan Kagan  
(301) 402-0131, Fax (301) 480-7843  
Email: [jk38m@nih.gov](mailto:jk38m@nih.gov)

- C. *HIV Research Branch*. Clinical research of strategies to treat adult primary HIV infection and complications; strategies to augment HIV immune responses and general host immunity.

Chief: Dr. Carla Pettinelli  
(301) 496-0700, Fax (301) 402-3171  
Email: [cp22n@nih.gov](mailto:cp22n@nih.gov)

- D. *Opportunistic Infections Research Branch*. Preclinical and clinical research to develop better therapies for treating and preventing HIV opportunistic infections.

Chief: Dr. Barbara Laughon  
(301) 402-2304, Fax: (301) 402-3171  
Email: [bl17u@nih.gov](mailto:bl17u@nih.gov)

- E. *Pediatric Medicine Branch*. HIV therapies in children and adolescents, strategies to reduce transmission from mother to infant or fetus.

Chief: Dr. James McNamara  
(301) 402-2300, Fax: (301) 480-4582  
Email: [jm74q@nih.gov](mailto:jm74q@nih.gov)

#### **Division of Allergy, Immunology, and Transplantation**

The Division of Allergy, Immunology, and Transplantation (DAIT) supports studies of the immune system in health and the cause, pathogenesis, diagnosis, prevention, and treatment of disease caused by immune dysfunction.

Director: Daniel Rotrosen, M.D.  
(301) 496-1886  
Email: [dr17g@nih.gov](mailto:dr17g@nih.gov)

- A. *Office of Epidemiology and Clinical Trials*. Methodologies to design, manage, and analyze clinical research and epidemiologic research of the etiology, prevention, and treatment of asthma, allergy, and autoimmune diseases.

Director: Ernestine Smartt  
(301) 496-7353, Fax: (301) 402-2571  
Email: [es23r@nih.gov](mailto:es23r@nih.gov)

- B. *Asthma, Allergy, and Inflammation Branch*. Asthma, atopic dermatitis, hypersensitivity reactions, rhinitis, sepsis, sinusitis, urticaria, molecular basis of hypersensitivity, basic studies of asthma and allergy mechanisms, new therapies for asthma and allergic diseases, epidemiology and prevention, phagocyte biology, and mechanisms of host defense.

Section Chief: Dr. Ken Adams  
(301) 496-8973, Fax: (301) 402-2571  
Email: [ka93x@nih.gov](mailto:ka93x@nih.gov)

- C. *Basic Immunology Branch*. Origin, maturation, and interactions of immune

cells, immune cell receptors, ligands, and cytokine biology, molecular basis of activation, antigen recognition, tolerance, and immune response regulation, hematopoiesis and stem cell biology, enhancement of vaccine effectiveness in neonates and adults and basic immunology of vaccines.

Chief: Dr. Helen Quill  
(301) 496-7551, Fax: (301) 402-2571  
Email: [hq1t@nih.gov](mailto:hq1t@nih.gov)

- D. Clinical Immunology Branch. Autoimmune diseases, primary immune deficiencies (not HIV), basic research of disease mechanisms, immunotherapy of disease processes, disorders mediated by lymphocyte products, and mucosal immunity.

Chief: Dr. Elaine Collier (acting)  
(301) 496-7104, Fax: (301) 402-2571  
Email: [ec5x@nih.gov](mailto:ec5x@nih.gov)

- E. Genetics and Transplantation Branch. Identification and characterization of immune regulation genes and use of this knowledge to potentiate or inhibit immune responses (therapeutic immunomodulatory agents); development of animal models of human diseases; manipulation of the immune response to enhance vaccine efficacy; application of knowledge about the regulation of immune response genes to problems of immune dysfunction, whether native or in transplantation; development and improvement of diagnostic and detection methods for infectious agents from nonhuman species being used for transplantation into humans (xenotransplantation); development and improvement of immunomodulatory agents to prevent and treat immune mediated rejection of nonhuman organs, tissues and cells when transplanted into humans; and clinical trials of new methods to decrease transplant rejection including methods to induce donor specific tolerance.

Chief: Dr. Stephen M. Rose  
(301) 496-5598, Fax: (301) 402-2571  
Email: [sr8j@nih.gov](mailto:sr8j@nih.gov)

## **Division of Microbiology and Infectious Diseases**

The Division of Microbiology and Infectious Diseases (DMID) supports research to control diseases caused by all infectious agents, except HIV, through basic investigation of microbial physiology and antigenic structure, pathogenesis, clinical trials of drugs and vaccines, and epidemiologic studies.

Director: Dr. Carole Heilman  
(301) 496-1884  
Email: [ch25v@nih.gov](mailto:ch25v@nih.gov)

- A. Bacteriology and Mycology Branch. Bacterial diseases: anthrax, actinomycete infections, enterococcal infections, legionellosis, Lyme disease, nosocomial infections, plague, rickettsial diseases (including Coxiella, Ehrlichia, and Rickettsia), sepsis, staphylococcal infections, urinary tract infections, vector-borne bacterial infections, zoonotic bacterial infections; fungi and fungal diseases: aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, Pneumocystis carinii, other primary and opportunistic fungal infections; antibacterial and antifungal drug resistance; host-pathogen interactions; genetics, molecular, and cell biology; medical bacteriology and mycology; microbial structure and function; development of vaccines, drugs, and diagnostics; clinical trials of antibacterial and antifungal agents; and application of proteomics and genomics to facilitate advances in the areas listed above.

Chief: Dr. Dennis M. Dixon  
(301) 496-7728, Fax: (301) 402-2508  
Email: [dd24a@nih.gov](mailto:dd24a@nih.gov)

- B. Biometry Branch. Primarily provides consultation on the design, conduct, analysis, and reporting of clinical, population, and laboratory investigations of infectious diseases; analyzes and interprets research data; researches statistical methods and manages a small grant portfolio to develop statistical methods relevant to infectious disease research; develops computer software to analyze data; provides services and consultation for computer programming, data management, and study coordination; and serves on

clinical trial data safety and monitoring boards

Acting Chief: Dr. Mark Vanraden  
(301) 496-7065, Fax: (301) 402-0804  
Email: [mv8e@nih.gov](mailto:mv8e@nih.gov)

- C. Clinical and Regulatory Affairs Branch. Prepares investigational new drug applications for drugs and vaccines developed by DMID contracts and the NIAID Division of Intramural Research and fulfills regulatory requirements of the FDA for all contract-supported DMID clinical studies.

Regulatory Affairs: Ms. Elizabeth Horigan  
(301) 402-2126  
Email: [eh14z@nih.gov](mailto:eh14z@nih.gov)

- D. Enteric Diseases Branch. Research areas: (1) diseases and organisms: astrovirus, Bacteroides, calicivirus, Campylobacter, Clostridium, Crohn's Disease, diarrhea, enterotoxins, Escherichia coli, gastroduodenal disease, ulcers, gastroenteritis, Guillain-Barré, Helicobacter pylori, Listeria, normal flora, commensals, norwalk virus, rotavirus, Salmonella, Shigella, Staphylococcus, Vibrio, Yersinia, Hepatic, hepatitis A, B, C, D, E, G and animal model viruses, transfusion-transmitted virus (TTV), viral hepatitis; (2) basic virology and bacteriology, genome sequencing, natural history and pathogenesis; (3) immunology of infectious diseases including mechanisms of recovery and persistence, protective immune responses and immunopathogenesis in animal models and humans; (4) vaccine research and development to prevent infection and control disease; (5) development and evaluation of adjuvants and vaccine vectors; (6) identification of new drug targets and their use to identify new drugs; (7) immunotherapeutic drug discovery and development; (8) epidemiology and transmission; (9) clinical studies and trials; (10) development of model systems to study infection and disease; and (11) characterization and exploitation of the role of normal flora in disease preventive therapy.

Chief: Dr. Leslye Johnson  
(301) 496-7051, Fax: (301) 402-1456  
Email: [lj7m@nih.gov](mailto:lj7m@nih.gov)

- E. Parasitology and International Programs Branch. Research areas: (1) protozoal infections, amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis, Helminth infections, cysticercosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes), Invertebrate vectors/ectoparasites, blackflies, mosquitoes, ticks, snails, mites; (2) parasite biology (genetics, genomics, physiology, and biochemistry); (3) protective immunity, immunopathogenesis, evasion of host responses; (4) clinical and epidemiologic studies of the natural history of tropical and parasitic diseases; (5) research and development of vaccines, drugs, immunotherapeutics, and diagnostics, and (6) vector biology and control; mechanisms of pathogen transmission.

Chief: Dr. Stephanie L. James  
(301) 496-2544, Fax: (301) 402-0659  
Email: [sj13y@nih.gov](mailto:sj13y@nih.gov)

- F. Respiratory Diseases Branch. Research areas: (1) viral respiratory diseases, including those caused by: coronaviruses, influenza, parainfluenza viruses, paramyxoviruses, respiratory syncytial virus; (2) bacterial respiratory diseases, including those caused by chronic obstructive pulmonary disease (Moraxella catarrhalis), cystic fibrosis (Pseudomonas aeruginosa and Burkholderia cepacia), Corynebacterium diphtheriae (diphtheria), groups A and B streptococcus, meningitis (Haemophilus influenzae and Neisseria meningitidis), otitis media, pertussis (Bordetella pertussis), pneumonia (Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae and Klebsiella pneumoniae); (3) Otitis media; (4) mycobacterial diseases, including those caused by: M. tuberculosis (tuberculosis), M. leprae (leprosy), non-tuberculous mycobacterial diseases; (5) development and licensure of vaccines and therapeutic agents for treating and preventing respiratory diseases; (6) maternal immunization; (7) basic research on the pathogenesis, immunity, structural biology, molecular genetics, and genomics of respiratory pathogens; (8) epidemiology and natural history of

respiratory pathogens ; (9) development of better and more rapid diagnostics; and (10) understanding the etiology and long-term health impact of respiratory pathogens in various populations.

Chief (acting): Dr. Ann Ginsberg  
(301) 496-5305  
Email: [ag73i@nih.gov](mailto:ag73i@nih.gov)

- G. *Sexually Transmitted Diseases Branch.*  
Development of diagnostics, drugs, topical microbicides, and vaccines; role of STDs in HIV transmission; role of HIV in altering STD natural history; molecular immunology; epidemiologic and behavioral research; adolescents and STDs; STDs and infertility; STDs and adverse outcomes of pregnancy; other sequelae of STDs; Genomics of sexually transmitted pathogens.

Chief: Dr. Penny Hitchcock  
(301) 496-0443, Fax: (301) 402-1456  
Email: [ph22k@nih.gov](mailto:ph22k@nih.gov)

- H. *Virology Branch.* Acute viral infections and zoonoses, dengue and other arthropod-borne viral diseases (mosquito-borne encephalitis, including West Nile, yellow fever, etc.), hantaviruses, hemorrhagic fevers (Ebola, Lassa, South African hemorrhagic fevers, etc.), measles, polio, coxsackie virus, and other enteroviruses, poxviruses, rabies, rubella; persisting viral diseases and viruses: adenoviruses, bornaviruses, coronaviruses, herpesviruses, parvoviruses, prion diseases; emergence of viral disease; mechanisms of replication, permissiveness, persistence, and latency; vaccines; immune protection and evasion and viral vectors; epidemiology and viral evolution; structure and function of viruses and viral proteins; molecularly targeted approaches to identify and characterize antiviral targets and agents; chemical design and synthesis of novel antiviral agents; in vitro screening and evaluation of antiviral activity; preclinical therapeutic and some prophylactic evaluations of human viral infections in animal models; clinical trials of vaccines and therapies for viral infections; research of civilian defenses for potential bioterrorist use of viruses; development of rapid diagnostic systems; and chronic fatigue syndrome.

Chief: Dr. Catherine A. Laughlin  
(301) 496-7459, Fax: (301) 402-0659  
Email: [cl28r@nih.gov](mailto:cl28r@nih.gov)

### **Other Research Topic(s) Within Mission of Institute**

For additional information on research topics, contact:

Dr. Gregory Milman  
National Institute of Allergy and Infectious Diseases  
(301) 496-8666  
Email: [gm16s@nih.gov](mailto:gm16s@nih.gov)

For administrative and business management questions, contact:

Ms. Mary Kirker  
Grants Management Officer  
National Institute of Allergy and Infectious Diseases  
(301) 496-7231  
Email: [mk35h@nih.gov](mailto:mk35h@nih.gov)

### **NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)**

The NIAMS supports research in arthritis and musculoskeletal and skin diseases. Such research is directed at basic understanding of the causes and development of rheumatic diseases, connective tissue diseases, musculoskeletal and skin disorders and diseases. Basic investigations involve immunology; purine metabolism; skeletal muscle structure, function, metabolism and physiology; the structure, function, production, biochemistry and physiology of collagen, elastin, and other proteins of connective tissue; metabolic and hormonal changes in bone; abnormalities in osteoarthritic cartilage; new treatments for fractures; the biomechanics of normal, arthritic and prosthetic joints; the structure, function, barrier properties, metabolism, and physiology of the skin.

For additional information about areas of interest to the NIAMS, please visit our home page at <http://www.nih.gov/niams>.

## Arthritis and Musculoskeletal and Skin Diseases

- A. *Rheumatic Diseases Branch*. Supports basic and clinical research in the normal function and components of connective tissue and the immune system and their dysregulation in rheumatic, genetic, and inherited diseases of connective tissue. The goals are increased understanding of the etiology and pathogenetic mechanisms involved in rheumatic and degenerative disease of the joints and in the translation of these basic research findings to prevention, diagnosis, and treatment of disease. The research supported by the Program utilizes approaches emanating from relevant areas of genetics, biochemistry, cellular and molecular biology, biophysics, enzymology, immunology, pathology, physiology, behavioral medicine, and epidemiology.

A description of other areas of research under investigation may be found at <http://www.nih.gov/niams/grants/ep3.htm>.

- B. *Musculoskeletal Diseases Branch*. Supports studies of the skeleton and associated connective tissues. Research areas supported through the Musculoskeletal Diseases Branch include bone diseases, bone biology, and orthopaedic research. Broad areas of interest include skeletal development, metabolism, mechanical properties, and responses to injury. Osteoporosis, a disease afflicting many of the Nation's growing population of older people, is particularly emphasized for investigation under this program. Among other diseases and skeletal disorders under investigation are osteogenesis imperfecta, a genetic disorder that leads to fragile, easily fractured bones; Paget's disease of bone, which results in irregular bone formation and subsequent deformity; genetic disorders of bone growth and development, such as osteopetrosis and the osteochondrodysplasias; vitamin D refractory diseases; and rickets and osteomalacia. Other studies focus on the causes and treatment of acute and chronic injuries, including carpal tunnel syndrome, repetitive stress injury, low back pain and clinical and epidemiological studies of osteoarthritis. The Program supports

development of new technologies with the potential to improve treatment of skeletal disorders and facilitate the repair of trauma in the normal skeleton. These include drugs and nutritional interventions, joint replacement, bone and cartilage transplantation, and gene therapy. In addition, bioengineering, sports medicine and musculoskeletal fitness are areas of special research emphasis.

A description of other areas of research under investigation may be found at <http://www.nih.gov/niams/grants/ep5.htm>.

- C. *Skin Diseases Branch*. Supports basic and clinical studies of the skin in normal and disease states. The wide range of skin diseases under study with NIAMS support includes keratinizing disorders such as psoriasis and ichthyosis, atopic dermatitis and other chronic inflammatory skin disorders, the vesiculobullous diseases such as epidermolysis bullosa and pemphigus, acne, and vitiligo.

A description of other areas of research under investigation may be found at: <http://www.nih.gov/niams/grants/ep6.htm>.

1. Determinations of drug effects.
2. Determinations of effects of other therapies, including occupational and physical therapy modalities, spinal manipulation, bracing, transcutaneous nerve stimulation, acupuncture, and topical agents (e.g., capsaicin).
3. Preventive strategies.
4. Development and validation of animal models for rheumatic, musculoskeletal (especially for herniated intervertebral disc and spinal stenosis), muscle and skin diseases.
5. Improvement and refinement of immunogenetic determinants of rheumatic diseases.
6. Development of novel and improved diagnostic methods and treatments for muscle, tendon, ligament, bone, and joint injuries, including overuse and repetitive motion disorders.
7. Devices and activities designed to prevent muscle, tendon, ligament, and joint injuries, including overuse and repetitive motion disorders.

8. Assessment techniques for musculoskeletal and skin diseases.
9. Functional and metabolic measures of the musculoskeletal system in normal, diseased and active states.
10. Development of novel implant designs, materials and surface coatings for musculoskeletal implants. Development of assessment strategies to detect implant failure, loosening, and osteolysis, and the development of novel technologies to prevent them.
11. Computer modeling, relevance to the musculoskeletal system.
12. Improved topical treatments of skin diseases and disorders.
13. Devices and computer programs for diagnosis or assessment of skin diseases.
14. Tissue culture models for skin diseases.
15. Artificial skin.
16. Photoprotective agents.
17. Improved treatment for bone diseases.
18. Measurement techniques for bone diseases.
19. Preventive measures for fractures.
20. Delivery systems for dietary supplements.
21. Novel delivery systems for therapeutic agents.
22. Development of novel or improved technologies for bone healing and repair. This includes, but is not limited to, the development of osteoinductive, osteoconductive, or a combination, technologies to facilitate bone healing/repair, and the development of improved or novel approaches to the use of autogenous, allograft, and bone graft substitutes.
23. Development of novel or improved technologies to facilitate the repair of articular cartilage, including, but not limited to cartilage cell transplantation, use of stem cells, biodegradable scaffolds, growth factors, and refinements of currently existing technologies.
24. Development of novel technologies to improve the diagnosis, prevention, and treatment of acute and chronic low back pain.

25. Development of novel assessment technologies for identifying biomechanical inputs on bone and cartilage tissue at the cellular level, and identification of the corresponding physiological response.
26. Development of novel technologies leading to the use of gene therapy for selected musculoskeletal diseases and injuries.
27. Development of novel, non-invasive technologies to assess joint tissues, including articular cartilage and subchondral bone.

### **Markers of Osteoarthritis**

The NIAMS seeks applications for the development and validation of standardized, sensitive assays for osteoarthritis markers in body fluids or tissue specimens. Osteoarthritis is the most prevalent musculoskeletal disorder, characterized by joint pain, tenderness, and functional disability. The percentage of Americans over 65 years of age is the fastest growing segment of the population, which is expected to reach 68 million people by the year 2010. A biochemical test for osteoarthritis would be particularly useful for early detection, assessment of disease severity and progression, and to monitor the effects of therapies.

Advances in the molecular biology, biochemistry, and metabolism of cartilage have stimulated the quest for appropriate markers of degradative and regenerative processes in osteoarthritis. Important new studies indicate that molecular fragments of cartilage-derived matrix molecules are present in the blood and joint fluid in osteoarthritis that have the potential to represent disease-specific markers. The increased rates of cartilage degeneration increase the concentration of matrix components in tissue and body fluids, thus reflecting changes in the rates of cartilage catabolism. Further, cartilage degeneration in osteoarthritis changes the type or structure of the molecules being synthesized by the chondrocytes. Thus, the presence of these neo-epitopes may be a marker of degenerative events within the tissue. Markers of metabolic changes in subchondral bone or other joint tissues in osteoarthritis are also be of potential interest.

The NIAMS is soliciting applications to test the potential application of a marker for osteoarthritis diagnosis, prognosis or severity

and the standardization of a clinically relevant test. Successful applicants will provide a rational approach for the development of a practical and reliable assay for osteoarthritis disease marker(s) and determination of the sensitivity and specificity of the marker(s) in patient populations. The applications must include the rationale for the selection of the marker to be employed in the study. If a battery of markers will be utilized the basis of this approach must be clear and well justified. The assay systems as well as the methods of sample collection, storage, and handling must be clearly delineated. Marker levels must be validated against other methods of monitoring osteoarthritis, such as imaging techniques. The expected outcome of these studies is an osteoarthritis test that can be used in larger scale human trials.

## **Muscle Biology, Exercise Physiology and Sports Medicine**

### **A. *Muscle Biology Branch.***

Supports research on skeletal muscle, its diseases and disorders, and its central role in human physiology and exercise. Topics include the molecular structure of muscle and the molecular mechanisms that produce force and motion. An aim is understanding the alterations in muscle resulting from increased exercise regimens and, conversely, the atrophy that follows immobilization during injury or illness. Some of the specific areas of research covered by the Muscle Biology Branch include Muscle Physiology, Molecular Architecture, Muscle Membranes, Muscle Development and Specialization, Musculoskeletal Fitness and Adaptive Biology, Muscle Diseases, and Sports Medicine, Muscle Injury and Muscle Repair. Areas that may be of interest to small businesses include but are not limited to:

#### **1. Muscle Structure and Function**

Research on the application of biochemistry, molecular, and cell biology to muscle biology, including studies of membrane structure, function, and biosynthesis, lipid metabolism, membrane models, membrane transport, sub-cellular organization, organelles, cytoskeletal components, and cell division. Development of new instruments and

methods to facilitate studies on muscle function and physiology. Specific examples might include, but are not limited to, the following:

- a. Development of methods and materials directed toward the solution of muscle cytoskeletal and membrane protein structures by x-ray diffraction, electron diffraction, and NMR spectroscopy.
- b. New methods for the purification and reconstitution of muscle membrane proteins.
- c. Development of monoclonal and/or recombinant antibodies to cytoskeletal and membrane proteins exhibiting high specificity and affinity and broad cross-species reactivity.

#### **2. Muscle Fitness and Sports Medicine**

- a. Improve measurement of muscle strength and balance, including refined instrumentation for biomechanical assessment of normal movement and posture.
- b. Develop quantitative methods of assessing postural perturbations and forces relevant to activities of daily living.
- c. Improve imaging and analytical techniques to measure skeletal muscle properties, (e.g., through MRI Imaging and Spectroscopy).
- d. Imaging techniques which allow simultaneous imaging of muscle morphology and metabolism and blood flow.
- e. Development of novel assays or modifications of currently existing assay of muscle metabolism for use with human biopsy samples.
- f. Develop biosensors to detect changes in pressure, temperature, or physiological parameters associated with muscular activity.
- g. Development of treatments for wound healing and improve general understanding of the natural healing process for muscle.

- h. Develop antioxidant interventions to prevent oxidative damage during muscle use and overuse.
  - i. Develop cell culture models for rapid testing of treatments for muscle injury and wasting.
3. Development and Genetic Diseases
- a. Develop animal models that mimic the pathophysiology of the genetic human muscle diseases.
  - b. Develop gene vectors (viral and non - viral), promoter and enhancer elements and related methodologies that could be used for in vivo and ex vivo gene therapy for muscular diseases.
  - c. Develop cell lines and tissue cultures for replacement of muscle that has been damaged or destroyed.
  - d. Develop markers for muscle satellite cells and use them to characterize availability for muscle repair.
  - e. Develop techniques, equipment, and software to enable improved imaging of muscle development and specialization.

#### **Other Research Topic(s) Within Mission of the Institute**

For additional information on research topics, contact:

##### *Rheumatic Diseases*

Dr. Susana Serrate-Sztejn  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
(301) 594-5032; Fax: (301) 480-4543  
Email: [ss86e@nih.gov](mailto:ss86e@nih.gov)

##### *Cartilage and Connective Tissue*

Dr. Bernadette Tyree  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
(301) 594-5032; Fax: (301) 480-4543  
Email: [bt16w@nih.gov](mailto:bt16w@nih.gov)

##### *Muscle Biology*

Dr. Richard Lymn  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
(301) 594-5128; Fax: (301) 480-4543

Email: [rl28b@nih.gov](mailto:rl28b@nih.gov)

##### *Skin Diseases*

Dr. Alan N. Moshell  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
(301) 594-5017; Fax: (301) 480-4543  
Email: [am40j@nih.gov](mailto:am40j@nih.gov)

##### *Orthopaedics*

Dr. James Panagis  
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##### *Bone Biology*

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#### **NATIONAL CANCER INSTITUTE (NCI)**

The NCI is the Federal Government's principal agency established to conduct and support cancer research, training, health information dissemination, and other related programs. As the effector of the National Cancer Program, the NCI supports a comprehensive approach to the problems of cancer through intensive investigation in the cause, diagnosis, prevention, early detection, treatment, rehabilitation from cancer, and the continuing care of cancer patients and families of cancer patients. To rapidly achieve the goal, NCI has developed a plan to: (1) sustain at full measure proven, productive research programs, (2) seize extraordinary scientific opportunities made possible by previous research discoveries, and

(3) create and sustain mechanisms that build the capacity to allow the scientific community to apply rapidly evolving discoveries and emerging technologies for the benefit of human health.

Many of the topics below are “open-ended” to encourage submission of innovative SBIR/STTR projects that fit within the mission of NCI. For additional information about areas of interest to NCI, please visit our home page at <http://www.nci.nih.gov>. The NCI small business site <http://www.cancer.gov/smallbusiness> may also be of interest.

### **Division of Cancer Biology**

The Division of Cancer Biology (DCB) plans and directs, coordinates, and evaluates a grant- and contract-supported program of extramural basic and applied research on cancer cell biology and cancer immunology, and cancer etiology, including the effects of biological, chemical and physical agents, in the promotion of cancer; maintains surveillance over developments in its program and assesses the national need for research in cancer biology, immunology and etiology; evaluates mechanisms of biological, chemical and physical carcinogenesis and subsequent tumor growth and progression to metastasis; tests for carcinogenic potential of environmental agents; serves as the focal point for the Federal Government on the synthesis of clinical, epidemiological and experimental data concerning biological agents relating to cancer; and maintains the necessary scientific management capability to foster and guide an effective research program. For additional information, please visit our home page at <http://www.nci.nih.gov/dcb/dcbhom.htm>.

A. *Biological Carcinogenesis*. The Biological Carcinogenesis Branch (BCB) supports research that seeks to determine the role of microbiological agents as factors or cofactors in the etiology of human and animal cancer. The biological agents of primary interest are DNA viruses, RNA viruses, AIDS and AIDS-associated viruses, although the research may encompass all forms of life including bacteria and other microbial agents associated with cancer and use animal models of cancer and cancer vaccines. A wide range of approaches are supported, including basic biochemistry and molecular biology of oncogenic and suspected oncogenic agents, viral oncogenes and

associated tumor suppressor genes, pathogenesis and natural history studies, animal models, and preventive vaccine research. The development of technologies to facilitate studies relating to biological carcinogenesis research is also encouraged. Specific research and technologies supported by BCB in this solicitation include but are not limited to the following:

1. Development of reagents, probes, and methodologies to evaluate the etiologic role of oncogenic viruses and other microbial agents (such as bacteria) in human cancer.
2. Development of novel in vitro culture techniques for oncogenic viruses or other microbial agents associated with or suspected of causing human cancer.
3. Development of sensitive, simplified diagnostic kits or reagents for the detection of oncogenic viruses or other microbial agents.
4. Development and characterization of animal models for studies of the mechanism of cancer induction by viruses or other microbial agents. The animals should faithfully mimic the human diseases associated with the virus or other microbial agent.
5. Development of methods (e.g., new-anti-microbial compounds, new vaccine approaches) to avert the induction of neoplasia in humans and animals by oncogenic viruses or bacteria.
6. Development of other novel technologies, methodologies or instrumentation to determine the role of biological agents, especially viruses, in the etiology of cancer.

B. *Cancer Cell Biology*. The Cancer Cell Biology Branch (CCBB) seeks to understand the biological basis of cancer at the cellular and molecular level. This research utilizes lower eukaryote and animal models, and animal and human tumor cells and tissues to analyze the mechanisms responsible for the growth and progression of cancer. Specific research and technologies supported by CCBB in this solicitation include but are not limited to the following:

1. Development of novel methods to study apoptosis.
  2. Development of methods to identify tissue-specific stem cells.
  3. Development of markers associated with specific cellular processes or differentiation.
  4. New techniques to transfer functional genes, proteins, antibodies, etc. into intact cells or organisms.
  5. Development of new in vitro cancer models which closely parallel in vivo conditions.
  6. Improved methods to isolate and preserve human cancer cells appropriate for research.
  7. New or improved technologies for efficient microdissection of tumor tissue sections. Among other uses, these approaches would be useful for isolation of DNA from tumor tissues at defined stages of tumor progression.
  8. Development of human tumor cDNA library banks to study gene expression in cancer.
  9. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
  10. Establishment of new or improved animal models or non-mammalian models (e.g., flies, worms) as research tools to study gene mutations important in human cancers. Among other uses, such models could be used to study the role of cancer genes or for analysis of complex traits.
  11. Generation of new inbred genetic animal models that transmit defective or altered cancer-related genes.
  12. Development of other novel technologies, methodologies or basic instrumentation to facilitate basic cancer research (research tools).
- C. Cancer Immunology and Hematology. The Cancer Immunology and Hematology Branch (CIHB) supports a broad spectrum of basic research focused on the earliest stages of hematopoiesis and tracing the molecular events that lead to the development of all the functional elements

of the immune system and, when errors occur, to the development of leukemias and lymphomas. Most research of interest falls into three major areas. The first is the immune response to tumors to include studies of all of the cells (T, B, NK, antigen-presenting, and other myeloid cells) and secreted molecules (antibodies and cytokines) of the immune system that can recognize and affect tumor growth. Emphasis is placed on the regulatory mechanisms responsible for the failure of immune response to eradicate most tumors under normal conditions, and the development of strategies to circumvent these mechanisms. A second major area of interest examines the biology of hematopoietic malignancies to describe the detailed reasons underlying cell's failure to respond to normal growth controls and to develop novel approaches to prevention or therapy. The third distinct area supported is the basic biology of bone-marrow transplantation, including studies of host cell engraftment, graft-versus-host disease, and the basis of the graft-versus-leukemia effect. Specific research and technologies supported by CIHB in this solicitation include but are not limited to the following:

1. Development of improved or novel monoclonal antibody technologies including improvements of methodologies for fusion, production of novel cells as fusion partners, selection and assay of antibody producing clones, and production of new and improved monoclonal antibodies.
2. Synthesis, structure and function of antibodies capable of reacting with tumor cells, agents that induce tumors, agents used in the treatment of tumors, and agents used in the treatment of tumors.
3. Development of in vivo animal models systems that can be used to study the immune response to tumors and the mechanisms of immunotherapy.
4. Development of technology for large-scale production of specific immune modulators (e.g., lymphokines).
5. Synthesis, structure and function of soluble factors that participate in, activate and/or regulate hematopoietic cell growth and the immune response

- to tumors, including interferons, other lymphokines and cytokines (interleukins), hematopoietic growth factors, helper factors, suppressor factors and cytotoxic factors.
6. Application of biochemical, molecular biological and immunological techniques for identifying tumor antigens that are good targets for the development of vaccine-type strategies of cancer immunotherapy.
  7. Development of techniques to enhance the immune response to tumors, including modification of tumor cells and/or antitumor lymphocytes to facilitate cancer vaccine strategies.
  8. Development of improved methodology for manipulating bone marrow inoculum to decrease the incidence of graft-versus-host disease without increasing the risk of graft failure or leukemic relapse.
  9. Development of improved methodology for increasing the number of peripheral blood stem cells available for harvest for use in transplantation, including improved methods of identifying and removing residual leukemic cells in the autologous transplant setting.
  10. Development of methods to identify and define human minor histocompatibility antigens.
  11. Development of novel techniques for antigen identification and protein identification in human tumor cells.
  12. Development of novel culture systems to improve the expansion of lymphocytes.
  13. Development of combinatorial cell culture research tools to better understand expansion of human hematopoietic stem cells.
  14. Development of improved techniques for computational simulation/modeling of biological processes involved in immunologic defenses against tumor cells such as signal transduction, cell cycle progression, and intracellular translocation.
  15. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer immunology and hematology.
- D. *Chemical and Physical Carcinogenesis.*  
The Chemical and Physical Carcinogenesis Branch (CPCB) supports basic and applied research concerned with cancers caused or promoted by chemical or physical agents. Carcinogenesis research is supported at the molecular level in areas such as the genetics of cell transformation, mutagenesis, tumor promotion, and DNA damage. Mechanistic studies are encouraged in areas such as metabolism, toxicity and physiological distribution of carcinogens, genetics and regulation of enzymes, biochemical and molecular markers, and organ and cell culture systems and animal models. Also of interest are studies on cancer etiology by environmental chemicals, tobacco consumption and exposure, nutritional hazards, alcohol, asbestos, silica, and man-made fibers. CPCB supports studies on endogenous exposure to steroid hormones and the generation of oxygen radicals during normal metabolism, studies on phytoestrogens and xenoestrogens and their impact on the metabolism of endogenous estrogens are also supported, and work on carcinogenicity/mutagenicity, testing procedures and the development of analytical technologies for use in carcinogenesis research. Specific research and technologies supported by CPCB in this solicitation include but are not limited to the following:
1. Development and validation of methods for food treatment, preparation, or processing that will reduce or eliminate carcinogen/mutagen content.
  2. Development of rapid analytical techniques for the qualitative and quantitative detection and screening of xenobiotics, chemical contaminants, and carcinogens/mutagens in human foods and biological and physiological specimens.
  3. Development of in vitro and in vivo models for basic studies of carcinogenesis in specific organ systems, such as the pancreas, prostate, ovary, central nervous system, kidney, endometrium, stomach, and upper aerodigestive tract.

4. Development of methods for the production of carcinogens, anticarcinogens, metabolites, biomarkers of exposure, oxidative damage markers, and DNA adducts, both labeled and unlabeled, which are neither currently available commercially nor offered in the NCI Chemical Carcinogen Reference Standard Repository. The production of these compounds, in gram quantities, is desired for sale/distribution to the research community.
  5. Development of methods for detection, separation, and quantitation of enantiomeric carcinogens, metabolites, adducts, and biomarkers of carcinogen exposure.
  6. Development of monoclonal antibodies that are specific for different carcinogen-nucleoside adducts and demonstration of their usefulness in immunoassays. Of particular interest are antibodies to alpha-beta unsaturated carbonyl compounds (such as acrolein and crotonaldehyde) which can form exocyclic nucleoside adducts with DNA, and immunoassays for carcinogen/protein adducts as potential biomarkers of exposure.
  7. Development of immunoassays using monoclonal antibodies that are specific for different polymorphs of Phase I and II carcinogen-metabolizing enzymes and repair enzymes. Included, but not limited to, are antibodies to the cytochrome P450 isozymes, glutathione S-transferases, and N-acetyl transferases.
  8. Development of rapid, sensitive, and quantitative assays for the identification and measurement of androgens, estrogens, phytoestrogens, and xenoestrogens in complex biological matrices.
  9. Development of rapid analytical techniques for the direct measurement of ligand-protein receptor interactions and determination of binding coefficients.
  10. Development of analytical instrumentation for the detection and quantitation of extremely low levels of Tritium (3H) or 3H and Carbon-14 (14C) from biological samples. Of particular interest is the development of small-sized, accelerator-based mass spectrometry equipment capable of measuring down to, or below, contemporary background levels of 3H and 14C that would make this sensitive technique more widely available to research groups. The design and development of technologically improved and miniaturized individual components, including ion source, sample preparation (autosampling apparatus), accelerator, and mass spectrometric detectors, are also solicited.
  11. Isolation and development, from natural sources and/or synthesis, of potentially anticarcinogenic flavonoids, isoflavonoids, lignans, Vitamin D analogs, hormonal agonists/antagonists, bioavailable protease inhibitors, and terpene compounds.
  12. Synthesis of selective suicide inhibitors of cytochrome P450 isoforms and selective arachidonic acid pathway inhibitors/enhancers for basic biochemical studies and anticarcinogenic potential.
  13. Development of invertebrate animal models (such as *Drosophila*, *C. elegans*, clam, and sea urchin) for the study of environmental chemicals and/or hormonal carcinogenesis.
  14. Development of more efficient and reliable methods of preserving valuable animal model gene stocks by innovative in vitro techniques.
  15. Development of a defined diet for support and maintenance of aquatic and marine fish models of cancer including but not limited to swordtail, zebrafish, medaka, mummichog, guppy, Fugu, and Damselfish.
  16. Development of serum free tissue culture media for aquatic and marine fish models of cancer.
- E. *DNA and Chromosome Aberrations*. The DNA and Chromosome Aberrations Branch (DCAB) seeks to study the genome at the DNA and chromosome level, including discovery of genes at sites of chromosome breaks, deletions, and translocations, DNA

repair, structure and mechanisms of chromosome alterations, epigenetic changes, radiation- and chemical-induced changes in DNA replication and other alterations, and analytical technologies. Specific research and technologies supported by DCAB in this solicitation include but are not limited to the following:

1. Development of new, improved technologies for characterization of chromosomal aberrations in cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for chromosome aberrations in cancer; spontaneous, chemical or radiation induced.
3. New or improved technologies to increase accuracy of karyotypic analyses of tumor specimens.
4. New or improved methods to mutate genes at specific sites, or to replace genes, in intact cells.
5. Development of novel gene technology (e.g., microarray, differential display technology) for measurement of differential gene expression levels and functional genomic studies.
6. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
7. Technologies for assaying for mammalian genes relevant to repair of damage induced by exposure of mammalian cells to ionizing and non-ionizing radiations, with special emphasis on human cells.
8. Methods/approaches to study the repair of DNA lesions induced by exposure of mammalian cells to ionizing radiations (both high- and low-LET).
9. Development and characterization of human cell lines with specific DNA-repair deficiencies.
10. Development of genetic constructs that utilize radiation-responsive regulatory genes to control the expression of targeted structural genes in mammalian cells.

F. *Mouse Models of Human Cancers Consortium.* The Mouse Models of Human Cancer Consortium is a program based in the Office of the Director, DCB. The Consortium has the important goal of providing mouse cancer model-related resources and infrastructure to the research community, in part through various outreach activities. The outreach requirement generates the need for innovative educational or informational materials that convey the content of Consortium meetings and symposia, or document hands-on workshops in which models or techniques that are pertinent to mouse modeling are demonstrated. The instructional materials may be CD-ROMs, videotapes, Web-based interactive programs, or other media.

G. *Structural Biology and Molecular Applications.* The Structure Biology and Molecular Applications Branch (SBMAB) focuses on structural and molecular studies to explore the processes of carcinogenesis and tumorigenesis. Areas of interest include structural biology, genomics, proteomics, molecular and cellular imaging, enzymology, bio-related and combinatorial chemistry, and bioinformatics, as they apply to cancer biology. Interests also include modeling and theoretical approaches to cellular and molecular dimensions of cancer biology. Specific research and technologies supported by SBMAB in this solicitation include but are not limited to:

1. Development of new technologies to facilitate the analysis and determination of the molecular structure of macromolecules associated with cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for gene identification.
3. Development of systems that will automate the technology of culturing or assaying single cells.
4. New or improved technologies for efficient microdissection of tumor tissue sections and the development of tissue arrays.

5. Improved extraction techniques for tumor specimens for subsequent DNA, RNA, and protein analyses.
  6. Rapid methods to isolate intact complexes of regulatory proteins and to separate and identify the proteins.
  7. New or improved technologies for the preservation of small amounts of DNA/RNA/protein samples
  8. Development of new techniques and vectors for transfer of genes, proteins, and antisense molecules into cells.
  9. Generation of software and computer models for the prediction of macromolecular structure and function.
  10. Development new methodologies for the generation and automation of tumor cDNA libraries.
  11. Development of bioinformatic tools for the study of cancer biology including facilitating genome data, gene "mining", cluster analysis and data base management.
  12. Development of novel gene technology (e.g., microarray, differential display technology) for measurement of differential gene expression levels and functional genomics studies.
  13. Development of novel proteomic tools for the analysis of protein expression in cancer biology.
  14. Combinatorial library approaches for gene function analysis.
  15. Computer based methodologies to assist in the understanding of signal transduction and cancer biology.
  16. Methodologies and techniques for the imaging of macromolecules in vitro and in vivo.
  17. Development of in vivo imaging technologies for developmental model organisms.
  18. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer biology.
- H. *Tumor Biology and Metastasis*. The Tumor Biology and Metastasis Branch (TBMB) supports research focused on the interaction of the tumor with its local environment, the mechanism of tumor cells' acquisition of aggressive malignant behavior, and the influence of hormonal factors on tumor progression. Special emphasis is given to the development of appropriate animal and cellular models of metastasis. Research in tumor biology includes studies on: (1) the role of cell adhesion molecules; (2) the role the extracellular matrix and the basement membrane in development, tissue morphogenesis, wound healing, invasion, and metastasis; (3) the role of cytoskeleton, and nuclear matrix in cell proliferation, migration, and invasion; and (4) studies on gap junctional structures. Research in tumor progression and metastasis includes studies on: (1) the role of oncogenes and tumor suppressor genes in angiogenesis, matrix degradation, and metastasis; (2) the glycobiology of epithelial cell surfaces and functional consequences of aberrant glycosylation on cell adhesion, tumor progression, and metastasis; and (3) the role of steroid hormones and their receptors in transformation, tumor growth, and in the development of hormone independence during tumor progression. Models utilized in these studies may include animals, tumor tissues/cells, their components or their products. TBMB also focuses on the role of steroid hormones and their receptors during tumor growth and progression. Specific research and technologies supported by TBMB in this solicitation include but are not limited to:
1. New technical strategies to identify and assess the function of components of the extracellular matrix.
  2. Development of new in vitro cancer models to study the pathology and biology of solid tumors and tumor bearing animals.
  3. Development of technologies to identify novel factors that modulate angiogenesis.
  4. Identification of genes associated with the process of metastasis.
  5. Development of improved techniques for computational simulation/modeling of biological processes involved in malignant transformation, persistence, or invasion, such as signal

transduction, cell cycle progression, and intracellular translocation.

6. Development of other novel technologies, methodologies or instrumentation to facilitate basic cancer research (research tools).

### **Division of Cancer Control and Population Sciences**

The Division of Cancer Control and Population Sciences conducts basic and applied research in the behavioral, social, and population sciences, including epidemiology, biostatistics, and genetics that, independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality. Laboratory, clinical and population-based research, and health care are translated into cancer prevention, detection, treatment, and rehabilitation activities that cross the life span and the entire process of carcinogenesis, from primary behavioral prevention in youth, to screening, treatment, and survivorship. For additional information, please visit our home page at <http://dccps.nci.nih.gov>.

A. *Epidemiology and Genetics*. The Epidemiology and Genetics Program supports research in epidemiology, biometry, genetic epidemiology, molecular epidemiology, nutritional epidemiology, infectious epidemiology, environmental epidemiology, computing methodology, and multidisciplinary activities related to human cancers. Topics of interest include:

1. Conversion, validation, and documentation of statistical software packages for use in genetic and general epidemiological analyses on microcomputers.
2. Methods for the detection of biological markers of human exposure, human susceptibility, or nutritional status for use in epidemiological studies.
3. Development of software for the guidance of biomedical researchers in the appropriate use of meta-analytic procedures including prompts for necessary data input, suggestions for the best analytic route to pursue, and examples using published data.
4. Development of banks of standard questions about cancer risk factors;

suitably referenced for prior use, validity, reliability, and with appropriate evaluation of index questions. The resource should accommodate either interviewer- or self-administered approaches with flexibility to accommodate requests of varying informational depth.

5. Development of geographical information systems with special visualization techniques for the simultaneous assessment of environmental exposures and health outcomes.
  6. Improvements in computer-assisted telephone interviewing technology. Such improvements should permit refinements such as branching, rechecking of previous responses, tallies or summaries of the sum of specific responses for comparison with response to a more general question, and the entry of text as well as codes.
  7. Development of online hypertextual tutorials on specific areas of biostatistics and epidemiology with appropriate sample problems using relevant data.
  8. Development of an improved indexing system for epidemiologic literature and for data banks listing research in progress.
  9. Development of educational interactive software packages on cancer genetics susceptibility for clinical/paramedic personnel as well as patients.
  10. Development of user-friendly interactive pedigree analysis software for microcomputers.
  11. Development of molecular genetic techniques/methods applicable to large-scale epidemiological studies.
  12. Development and maintenance of a repository for unreported data on molecular/genetic polymorphisms.
  13. Development of educational intervention software packages for women and minorities exposed to occupational carcinogens.
- B. *Multimedia Technology and Health Communication in Cancer Control*. A major objective of DCCPS is to plan and conduct

extramural, grant-supported programs of cancer prevention and control research in medical and community settings that focus on biomedical and behavioral factors that alter cancer risk. Toward this effort, the Multimedia Technology and Health Communication Program promotes innovative ways of translating cancer research into interventions, programs, systems, networks, or products needed by health care professionals or the public to reduce cancer risks, provide treatment options, or address the needs of cancer survivors.

Grant applicants are required to develop, implement, and test the effectiveness of new or existing models of behavior modification or informational/educational applications using computer applications, advanced telephone technologies, videos, cable and broadcast television, radio, virtual reality, animation, digital imaging, smart cards, the Internet or the World-Wide-Web in the following categories:

1. Behaviors Associated with Cancer Risk
  - a. Nutrition Interventions: products or programs that promote cancer-reducing habits.
  - b. Smoking and Tobacco Cessation Interventions: products or programs that prevent, or promote smoking cessation among high-risk populations, especially young adults.
2. Cancer Genetics
  - a. Decision-making programs for families and individuals.
  - b. Information products for professionals on the psychosocial, ethical, and legal issues associated with cancer genetics.
3. Communication Techniques
  - a. Population-sensitive screening, assessing, monitoring, educational or training tools.
  - b. Communication approaches to use with persons with specific cancers, i.e., breast, head, neck, skin or prostate cancer.
4. Complementary Medicine Approaches
  - a. Mind/body products that improve the quality of life of persons with cancer or cancer survivors.
5. Innovative Alternative Teaching Methods
  - a. Cost and time-effective alternative teaching methods or games that promote the comprehension of cancer prevention and control.
6. Survivorship and Quality of Life Issues
  - a. Interactive programs that help resolve cancer survivor issues.
  - b. Products or programs to promote physical and emotional well-being that increase quality of life.
7. Systems for Primary Care Professionals and Oncologists
  - a. Patient screening, assessment, management or tracking programs.
  - b. Training programs for use by primary care providers and train the trainer programs.
  - c. Interactive curriculum modules, CME courses, training, or screening/ assessment programs for health professionals located in remote areas or where insufficient staff is available.
8. Systems for the Public
  - a. Cancer education, information, prevention, or screening and assessment programs or products for use by the public.

### **Division of Cancer Treatment and Diagnosis**

The Division of Cancer Treatment and Diagnosis (1) plans, directs and coordinates a program of extramural preclinical and clinical cancer treatment research as well as research conducted in cooperation with other Federal agencies with the objective of curing or controlling cancer in man by utilizing treatment modalities singly or in combination; (2) administers targeted research and development programs in the area of drug development, diagnosis, biological response modifiers, medical diagnostic imaging, and radiotherapy development; and (3) serves as the national focal point for information and data on experimental and clinical studies related to

cancer treatment and for the distribution of such information to appropriate scientists and physicians; and (4) plans, directs and coordinates an extramural program of basic and applied research conducted at cancer centers and through the organ systems program.

A. Cancer Diagnosis. The Cancer Diagnosis Program (CDP) supports the development of technologies, reagents, instrumentation, and methodologies to improve cancer diagnosis or prognosis or to predict or assess response to therapy. This does not include technologies for imaging of patients. CDP also supports the adaptation or improvement of basic research technologies for use as clinical tools. Technologies supported by CDP may be designed to work with tissues, blood, serum, urine, or other biological fluids. Technologies supported by CDP include but are not limited to the following:

1. Technologies for comprehensive and/or high throughput analysis of molecular alterations at the level of DNA, RNA, or protein. Includes for example, mutation detection systems, gene expression arrays, high throughput proteomics (including post-translational modification and protein-protein interactions and methods for protein quantitation).
2. Micro-electro mechanical systems (MEMs) for the analysis of DNA, RNA, or protein (e.g., microcapillary systems, lab on a chip applications, microseparation technologies).
3. Mass spectrometry for the analysis of nucleic acids or proteins.
4. Discovery and development of new or improved diagnostic markers or probes targeting changes in DNA, RNA, or proteins, including the generation of molecular diversity libraries by phage display and other combinatorial techniques, and affinity-based screening methods.
5. cDNA library technologies, including improved methods for generating high quality cDNA clones and libraries and methods for generating high quality cDNA from tissues (including archived specimens).
6. Resources for clinical research.

- a. Instruments, technologies or reagents for improved collection, preparation, and storage of human tissue specimens and biological fluids.
  - b. Improved methods for isolation and storage of DNA, RNA, or proteins.
  - c. Tissue and reagent standards: development of standard reagents such as representational DNA, RNA, and proteins and standard tissue preparations to improve the quality of or facilitate the validation of clinical laboratory assays.
  - d. Methodologies for directed micro-sampling of human tissue specimens, including for example, new or improved methodologies for tissue microarrays.
7. Tissue preservation: fixatives and embedding materials or stabilizers that preserves tissue integrity and cellular architecture and simultaneously allows molecular analysis of DNA, RNA, or proteins.
  8. Bioinformatics
    - a. Methods for acquisition and analysis of data associated with molecular profiling and other comprehensive molecular analysis technologies, including for example, analysis of microarray images and data as well as methods to combine, store and analyze molecular data produced by different techniques (e.g. combined analysis of proteomics and gene expression data).
    - b. Methods for collecting, categorizing or analyzing large data sets containing pathology data or histological images and associated clinical or experimental data, including for example, tumor marker measurements, tissue microarray data, and other relevant biological information.
    - c. Software/algorithms to interpret and analyze clinical and pathology data including methods that relate data from clinical databases to external data sources. Includes for example, neural networks, artificial

intelligence, data-mining, data-trend analysis, patient record encryption protocols, and automatic diagnostic coding using standard nomenclatures.

- d. Informatics tools to support tissue procurement and tissue banking activities.
- 9. Statistical methods and packages designed for data analysis including correlation of clinical and experimental data.
- 10. Automated Cytology
  - a. High resolution image analysis for use with specimens (e.g., blood, tissues, cells) and tissue microarrays.
  - b. Instrumentation including microscopy and flow cytometry.
  - c. CGH, FISH, immunohistochemical staining and other hybridization assays using probes with fluorescent or other novel tags.
  - d. Methods for single cell isolation and sorting.
  - e. Methods for single cell classification and analysis.
- 11. Instrumentation for the detection and diagnosis of tumors, including endoscopy and magnetic resonance spectroscopy (MRS).
- 12. Immunoassays using monoclonal, polyclonal, or modified antibodies. Affinity-based binding assays using libraries of aptamers including chemical ligands, small peptides or modified antibodies.

For additional information about areas of interest to the CDP Technology Development Branch, visit our home page at: <http://www-cdp.ims.nci.nih.gov/tdb.html>.

B. Biochemistry and Pharmacology.

Preclinical studies designed to improve cancer treatment in the following areas: Discovery of new drugs and treatment strategies, selective targeting, development of new preclinical models, pharmaceutical development, and toxicologic evaluations. Emphasis is on molecular targeted approaches. In addition to the topics below,

Biochemistry and Pharmacology sponsors special initiatives for Small Business Innovation Research (SBIR) and Small Technology Transfer Research (STTR) programs. For additional information, please visit our home page at <http://dtp.nci.nih.gov> and select "Funding."

1. Drug Discovery

- a. Design and synthesize novel compounds for evaluation as potential anticancer agents. Synthesize simpler analogs of complex antitumor structures that retain antitumor activity.
- b. Develop computer modeling and biophysical techniques such as x-ray crystallography and NMR spectroscopy.
- c. Design prodrugs of anticancer agents that are selectively activated in cancer cells.
- d. Discover new anticancer agents aimed at relevant targets that exploit unique properties of tumors, that induce or modulate apoptosis, or that induce or modulate differentiation.
- e. Design and synthesize anticancer prodrugs, latent drugs, or modifiers of cancer drug metabolism or excretion.
- f. Develop ways to produce adequate quantities of promising natural products or natural product derivatives through total synthesis.
- g. Develop scale-up technology for the synthesis of materials with promising anticancer potential.
- h. Develop chemical libraries for anticancer drug screening programs. The generation of small molecular weight libraries (<700 MW, e.g., non-polymeric organic molecules, transition-state analogs, cyclic peptides, peptidomimics) is encouraged.
- i. Develop array technologies for drug discovery.

2. Drug Evaluation

- a. Develop and evaluate anti-metastatic and/or anti-

angiogenesis agents or strategies in appropriate model systems.

- b. Develop and evaluate anticancer gene therapy in appropriate model systems. The development of new gene delivery approaches is encouraged.
- c. Develop novel or improved in vitro and in vivo test systems. There is a special need for new types of in vivo tumor models, such as orthotopic tumor models, models using transgenic or knockout animals, models for AIDS-associated malignancies, and models to evaluate agents that induce differentiation or apoptosis.
- d. Develop and evaluate rapid, cost-effective surrogate endpoints to predict clinical efficacy.
- e. Develop strategies to detect, prevent, or overcome drug resistance.
- f. Develop novel treatment strategies such as extra corporeal treatment.
- g. Develop new assays based on molecular targets, especially those that may be amplified or altered in cancer cells. For example, develop assays for agents that interact with oncogenes, suppressor genes, signal transduction pathways, transcription factors, promoters. Assays based on molecular targets that are adapted for high volume screening of chemical libraries are especially encouraged as well as in vivo models, which can be used for "proof of concept" (i.e., validating the selectivity of the agent for the target).
- h. Develop cost-effective and useful techniques to improve in vitro cell culture methodology, such as the development of automated systems, serum-free media, or carbon dioxide-free buffering systems to stabilize cell culture performance.
- i. Identify and employ novel targets for antitumor drug discovery utilizing non-mammalian genetically defined organisms,

such as fruit flies, worms, zebrafish and yeast.

- j. Develop array technologies for assays to evaluate activity.

### 3. Pharmaceutical Development

- a. Develop new methods to improve drug solubility for administration of promising antitumor compounds.
- b. Develop bioavailable alternatives to the intravenous delivery of cytotoxic chemotherapy.
- c. Develop improved methods to reduce thrombophlebitis and other related side effects observed following intravenous injection of some anticancer drugs.
- d. Develop new and innovative techniques for sterilization of parenteral dosage forms.
- e. Develop in vitro and in vivo models to predict human oral bioavailability of anticancer drugs.
- f. Develop practical delivery systems to deliver anticancer drugs to specific target sites.

### 4. Toxicology and Pharmacology

- a. Develop biochemical response profiles of specific target organs (e.g., bone marrow, gastrointestinal tract, liver, kidney, heart, lung) to permit rapid identification of toxic effects resulting from anticancer drug administration.
- b. Develop in vitro and/or in vivo tests for estimation and prediction of gastrointestinal toxicity, neurotoxicity (central and peripheral), cardiotoxicity, hepatotoxicity, nephrotoxicity and pulmonary toxicity.
- c. Correlate in vivo and in vitro models for organ toxicity as described above in 4b. Validate for various anticancer drugs.
- d. Develop drug metabolism (Phase I and Phase II) profiles for anticancer agents in human, mouse, rat and dog liver S-9, microsomes and slices.

- e. Develop systems to identify toxic effects of drugs by characterizing reactions with biomolecules or receptors.
  - f. Develop in vitro tests to detect, qualify and quantify toxic effects of antineoplastic drugs. Develop techniques for determining individual variations in drug responses due to genetic polymorphisms or other factors.
  - g. Develop a human somatic cell mutagenesis system.
  - h. Develop personal computer programs for pharmacokinetics models capable of predicting drug behavior in humans from preclinical pharmacokinetics data in mice, rats, dogs, and non-human primates.
  - i. Investigate and develop techniques for relating specific enzyme activities (both catabolic and anabolic) to body sizes of different species.
  - j. Investigate techniques that would allow parameters, e.g.,  $K_m$  and  $V_{max}$  for enzymes, to be scaled from preclinical to clinical models.
  - k. Develop analytical strategies applicable to the quantitation of potent anticancer drugs in biological fluids at the pg/ml level, e.g., Halichondrin B and Bryostatin.
  - l. Develop non-invasive techniques to determine drug distribution in various animal models.
  - m. Develop gene array technology to determine normal (untreated) and toxicity (cancer drug treated) profiles utilizing samples from various cells and animal tissues.
  - n. Evaluate interspecies transporter distribution and its impact on pharmacokinetic parameters, e.g., the impact of pharmacogenetic variation in biodistribution.
  - o. Determine optimal pharmacokinetic sampling schedules for use in dose titration/pharmacodynamic assessment by integrating information such as pre-clinical pharmacokinetic data, physico-chemical drug properties and mechanism of action.
  - p. Determine which mouse/rat strains provide the most relevant data predict clinical situations (e.g., according to class of compound or mechanism of action).
  - q. Develop an in vitro/in situ system for high throughput drug screens for oral bioavailability.
  - r. Development and delivery of organ specific chemo-protective agents.
5. Animal Production and Genetics
    - a. Investigate alternatives to expensive barrier systems for exclusion of pathogens from rodent colonies, e.g., by use of micro-isolator cages, and evaluate their performance.
    - b. Develop and evaluate specialized shipping containers for pathogen-free animals.
  6. Natural Product Discoveries. For the purposes of topics a, b, c, and e, examples of natural products in development are: Bryostatin, dolastatin 10, and halichondrin B. Note that execution of projects in most of these topic areas will require collaboration with countries where the source organism was originally collected.
    - a. Investigate new biological methods, such as tissue culture, genetic engineering, aquaculture, hydroponics, etc., for the production of natural product potential anticancer or anti-HIV agents.
    - b. Develop new systems of large-scale production using biotransformation, tissue or cell culture, biotechnology, modification of the chemical ecology of producing organisms, etc., in order to produce the large quantities of anticancer or anti-HIV drugs needed for preclinical or clinical development.
    - c. Investigate newer methods of isolation and purification, such as super-critical fluid extraction and

chromatography, centrifugal countercurrent chromatography or affinity-based separations, in the isolation and purification of natural products with anticancer or anti-HIV activity.

- d. Develop methods for the isolation, purification, identification, cultivation, and extraction of microorganisms from unusual marine or terrestrial habitats for antitumor and anti-HIV screening. Examples are gliding bacteria, psychrophilic, barophilic, endophytic, thermophilic, and tropical canopy organisms.
- e. Develop simple immunoassays that can be used to monitor the levels of natural products of interest in simple extracts of the relevant raw material. These assays should be capable of being developed for use "in the field" and also in developing countries.
- f. Develop techniques for the study of non-culturable organisms in order to identify antitumor agents.

#### 7. Data Management Systems

- a. Develop data support systems for chemical library programs.
- b. Develop bioinformatic tools to accelerate the identification, functional understanding and validation of drug targets.
- c. Develop "data mining" strategies such as neural networks.

- C. Cancer and Nutrition. Research to improve the methodology of nutritional assessment in a cancer population. Innovative approaches to evaluate the contribution of nutritional status to response to cancer treatment.

1. Research to improve the methodology of nutritional assessment in a cancer population.
2. Develop means to evaluate the contribution of nutritional status to response to cancer treatment.

- D. Clinical Treatment Research. Clinical research studies designed to improve cancer treatment. Emphasis is on clinical

trials for the evaluation of new therapeutic agents, development of assay systems to measure patient response to chemotherapy, development of prognostic assays, and development of methods of analysis and management of clinical trials data.

#### 1. Evaluation of New Cancer Therapies

- a. Conduct clinical trials for the evaluation of new therapeutic agents or modalities of treatment employing drugs, biologics or surgery.
- b. Clinical trials using "unconventional therapies", including, but not limited to, behavioral and psychological approaches, dietary, herbal, pharmacologic and biologic treatments, and immuno-augmentative therapies.
- c. Development and evaluation of new clinical approaches using gene transfer or gene therapy technologies.
- d. Development and evaluation of new clinical approaches using tumor associated antigens or vaccines in order to enhance immunogenicity.
- e. Develop and characterize novel chemical compounds that may be useful anticancer agents, either alone or in combination with other modalities such as radiotherapy.
- f. Develop techniques to lessen the toxicity of existing anticancer treatments.
- g. Develop new techniques for the delivery of anticancer agents that will maximize therapeutic effects and minimize toxicity.
- h. Develop new surgical techniques or tools or improve existing techniques that are/may be utilized in cancer treatment.
- i. Characterize and produce clinical grade monoclonal antibodies to detect and treat malignancies.

#### 2. Development of Prognostic Assays to Monitor Patient Response to Therapies

- a. Develop assay systems to measure the response of human tumors to chemotherapy or biologics.
  - b. Characterize drug resistance mechanisms and design methods to overcome clinical drug resistance.
  - c. Develop assays for prognostic factors to identify patient subsets who may benefit from specific cancer treatment therapies.
  - d. Development of assays to assess effects of agents on specific molecular targets in clinical studies.
  - e. Develop new techniques for relating past preclinical information to past clinical results for prediction of future useful clinical agents from future preclinical data (both in vitro and in vivo).
3. Clinical Trials Informatics
- a. Develop new tools and methodologies for the analysis of clinical trials results.
  - b. Develop new informatics tools to facilitate clinical trials data entry from the bedside and coordination of data entry and transmission throughout the institution and to other collaborating institutions or organizations.
  - c. Development of novel web-based approaches to clinical trials informatics for transmission of data to NCI or other organizations. Topics include point of treatment data capture and reporting, electronic protocols, OLAP (On-line Analytical Processing), support for the Common Toxicity Criteria, and drug accountability support.
  - d. Develop new interchange standards, based on technologies such as XML, for sharing data among heterogeneous systems. Specific applications areas include, Adverse Event Reporting, Case Report Forms.
  - e. Develop new tools for support of Common Data Elements.
  - f. Develop new approaches for interface with electronic medical records, with intent to streamline data reporting, registration, and toxicity reporting of Clinical Trial information.
- E. *Diagnostic and Medical Imaging Systems.*  
The development of imaging technology and in vivo imaging methods as required for research or clinical investigations using either pre-clinical models or human subjects. The research scope includes: (1) diagnostic imaging with ionizing or non-ionizing radiation and/or any other types of in vivo imaging technology or imaging methods; and (2) research related to the biological and health effects of diagnostic and/or combined diagnostic/therapeutic procedures. Suggested areas may include:
1. Development of in-vivo instrumentation and contrast enhancement methods for non-invasive and minimally invasive imaging/spectroscopy methods, including imaging investigations at different resolution, spectral and temporal scales as required at both the anatomical and cellular/molecular level. Methods include: (1) molecular imaging, (2) functional imaging, (3) anatomical imaging and (4) combined modality imaging. Non-invasive imaging methods include transrectal, transvaginal, and endoscopic probes. Minimally invasive methods include the use of interventional techniques such as image-guided surgery or image-guided biopsy or therapy. Physical probes or implanted devices that allow imaging and/or spectroscopy measurement in vivo are also included. Comparisons with invasive procedures are appropriate for validation of imaging methods.
  2. Developments of imaging system hardware and software components and other equipment that augment in vivo imaging/spectroscopy modalities, (i.e., X-ray, ultrasound, magnetic resonance, nuclear medicine, and optical or other imaging/spectroscopy technologies).
  3. Development and evaluation of contrast methods or contrast enhancement agents, both intrinsic and extrinsic. These may be needed for all

of the above in vivo imaging/spectroscopy modalities.

4. Development and evaluation of computer hardware and software for medical imaging, such as computer workstations, image processing methods, and informatics methods for image interpretation, image perception, and related outcome analysis.
5. Development and evaluation of image guided tools and methods for biopsy, surgery, therapy (including non-sealed sources), imaging means for monitoring and verification of treatment fields before and/or during all modes of therapy, including therapy response.
6. Research in radiation biology and radiation physics relevant to in-vivo imaging/spectroscopy methods.

F. *Radiation Research*. The Radiation Research Program (RRP) supports basic, developmental, and applied (clinical) research related to cancer treatment utilizing ionizing and non-ionizing radiations. Therapeutic modalities include photon therapy, particle therapy, photodynamic therapy (PDT), hyperthermia, radioimmunotherapy (RIT), and boron neutron capture therapy (BNCT). Radiation research encompasses a range of scientific disciplines including basic biology, chemistry, physics, and clinical radiation oncology. Topics of interest include, but are not limited to the following areas:

1. Develop devices for delivering radiation therapy or related therapies, including software related to treatment delivery, devices for patient positioning, and quality assurance for the following devices: (a) ionizing radiation, particularly for 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT); (b) ensuring reproducible patient setup and immobilization, particularly for 3DCRT and IMRT; (c) PDT; (d) hyperthermia; (e) RIT; and (f) epithermal neutron sources for BNCT.
2. Develop devices for dosimetry: (a) ionizing radiation; (b) PDT, particularly those capable of measuring light doses at depth in tissues; (c) thermometry for

hyperthermia, particularly non-invasive thermometry; (d) RIT; and (e) BNCT.

Devices may include chemical, solid state, film, biological, or ionization systems to detect or read out exposures. Accuracy, precision, and linear response is essential over the range of doses and temperatures employed in the research laboratory and/or in the clinic, depending on their intended use. Devices for thermometry during hyperthermia treatment must give accurate readings with the heating device(s) with which they are to be used.

3. Develop drugs to make radiation therapy or related therapies more effective: (a) chemical modifiers of radiation response, particularly small molecules and gene-based therapies; (b) photosensitizers for PDT; (c) sensitizers for use with hyperthermia; and (d) boron-containing compounds for BNCT.

4. Develop drugs to prevent, reduce, or reverse normal tissue response, especially the late effects that develop months or years after therapy.

Compounds that are based on a rationale for achieving a therapeutic gain (an improved differential response between tumor and normal tissue) are of greatest interest. Enhancement of response must be achieved at radiation doses and treatment schedules employed clinically.

5. Develop predictive assays and monitors of response to therapy employing radiation, PDT, hyperthermia, BNCT, or RIT. Tools to identify patients that would benefit from specific therapeutic approaches are needed.

G. *Biological Response Modifiers (BRM)*. Research on agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells with resultant therapeutic benefits. Both preclinical and clinical investigations are conducted on the utility of a wide variety of natural and synthetic agents and on biological manipulations of immunological and non-immunological host mediated, tumor-

growth controlling mechanisms in cancer therapy.

In addition, development of new approaches to modify host responses to the human immunodeficiency virus (HIV) is included in the scope of this announcement.

Studies are encouraged which utilize in vitro assays and/or animal model systems to investigate mechanisms of BRMs. Examples of innovative research that would be responsive to this solicitation include:

1. Application of observations describing shared receptors and mediators between the neuroendocrine and immune systems in studying immunobiology and immunotherapy of cancer or AIDS.
2. Evaluation of molecular genetic approaches to discovery of new therapeutic agents, delivery of BRMs, or development of gene therapy.
3. Studies of new agents active in inhibiting the development and/or reversing, multidrug resistance at the genetic and immunological level.
4. Development of improved techniques to synthesize, screen and develop new oligonucleotides for anti-oncogene or anti-viral effects.
5. Improvement in cell-culturing techniques, e.g., by developing automated cell culture systems, specialized media, or improved methods to induce activation, proliferation or differentiation.
6. Determination of new antitumor therapeutic approaches with maturation, differentiation or growth properties.
7. Development of new procedures or reagents for the modulation of the suppressor arm of the immune system in experimental models, directed towards successful immunotherapy.
8. Improvement of tumor-associated antigens or vaccines in an attempt to enhance immunogenicity.
9. Development of novel in vitro assays for the primary screening of BRMs.

## Division of Cancer Prevention

The Division of Cancer Prevention (DCP) directs an extramural program of cancer prevention research including chemoprevention, nutritional science, genetic and infectious agent, early detection including biomarker development and validation and biometry for the Institute. DCP also supports research training and career development in cancer prevention and early detection and coordinates community-based clinical research in cancer prevention and dissemination of cancer treatment practice through a consortium of community clinical centers. For additional information, please visit our home page at <http://dcp.nci.nih.gov/>.

A. *Prevention.* Research studies to identify, evaluate, and implement techniques and approaches for the prevention and early detection of cancer. Those studies capable of achieving these objectives with minimal risk and cost are preferred.

1. Chemoprevention. Studies in which naturally occurring or synthetic agents are identified, or further evaluated for efficacy or safety. Studies involving in vitro assays with cell transformation systems, in vivo assays involving animals models to evaluate agents against typical carcinogenic agents at specific sites, and studies involving clinical chemistry measurement of agents in sera or other biological fluids are of highest program relevance. Studies aimed at improving future research designs for chemopreventive trials; providing additional biological understanding, identification and evaluation of modulation of quantitative or qualitative biological endpoints, and/or markers for surveillance of compliance will also be considered. Examples of tests might include measurements of biochemical parameters, cytological screening techniques, in vitro studies of suppression of oncogene protein products, in vitro toxicological studies, and synthesis of novel chemopreventive agents based on structure/activity relationships.
2. Diet and Nutrition. Studies that aim to reduce the incidence of cancer through dietary modification, which may include additions, deletions, or substitutions of

foods or dietary factors. Studies aimed at dietary assessment and measures of compliance to the dietary modification are relevant to these dietary modification studies. Studies that can provide further understanding of the relationship between dietary components and cancer risk and the influence of dietary changes on biochemical indices, hormonal milieu and immune function will also be considered.

- B. Community Oncology. Introduction, application, and evaluation of effective and practical cancer control intervention programs in community settings. Primary emphasis is on the integration and involvement of community physicians and allied health professionals in cancer control efforts and the promotion of linkages between community practitioners/hospitals and other regional resources for cancer control.

Objectives are to: (1) reduce the time between research advances in prevention, detection, and patient management and their application in community settings; and (2) expand extend the cancer care knowledge and applications bases; and (3) evaluate new detection and diagnostic methods for specificity, sensitivity, reliability, validity, safety, feasibility and cost when applied to defined or target populations. This may include screening research as well.

- C. Rehabilitation and Continuing Care. Development and evaluation of rehabilitation or continuing care strategies which directly enhance functioning of patients with cancer or which contribute to understanding of factors impacting utilization of supportive services by cancer patients. Clinical applications include development and testing of interventions to enhance multidisciplinary approaches to cancer rehabilitation, and research on effective symptom management (e.g., cancer-related pain, fatigue, nausea, mucositis). Areas of general program interest include innovative approaches to measuring and enhancing quality of life of cancer patients; research to investigate and enhance clinical decision-making by both patients and physicians; and studies of the impact of individual preferences for health

care outcomes and their impact on cancer prevention practices in persons without cancer and on treatment decisions in patients with cancer.

- D. Early Detection and Screening. New diagnostic or screening methods for early detection of cancer, especially for asymptomatic patients. Detection methods can include any cancer site, although there is more interest in the common cancers, such as those of the lung and colon. Methods should be cost beneficial and applicable in a clinical setting.
1. Studies which identify and document new databases relevant to early cancer detection and propose using new and experimental analytical techniques.
  2. Analyses of long term follow up data from completed studies for potential new interpretations based on the passage of time.
  3. Studies which propose to develop and evaluate new detection techniques and measures for sensitivity specificity, reliability, validity and safety.
  4. Determinations of the cost/benefit or risk/benefit ratios of cancer screening and detection methods when applied in defined or target populations.
  5. Currently, the most commonly used method to detect prostatic cancer is the digital rectal examination. Devise and manufacture like-like modes for use in training for the early detection of prostate cancers by physical examination. Various models would be necessary. They would include, but not limited to the following disease states: (1) absence of disease (normal model); (2) benign prostatic hypertrophy; (3) prostatitis; (4) Stage B1 prostatic cancer (T2a); (5) Stage B2 prostatic cancer (T2b); and (6) Stage C prostatic cancer (T3z, T3b, and T4).
  6. Development of products that aid the systematic collection and transport of specimens used for the early detection of cancer, including devices for the collection and transport of urine, serum, fecal material, and other potential materials.
  7. Develop computer utility programs that can increase the clinical uses of

existing programs commonly found in medical offices creating age-sex registries, predicting population risks, determining screening needs of patients, reminder systems, etc.

8. Develop personal computer programs that can be used to determine population risks and the effect of interventions. These programs might also be adopted to the concept of Community Oriented Primary Care.
9. Use of ultrasonography with color flow imaging for the early detection of cancer. Research on the use of ultrasonography with color flow imaging (US-CFI) for the early detection of cancer of the ovary, breast and/or prostate. Emphasis should be given to the ability of the US-CFI to differentiate between malignant and benign disease at these sites. Criteria for the discrimination of malignant from benign disease would be developed as well as performance characteristics of this method, particularly for breast and prostate. Studies on symptomatic populations should yield sensitivity, specificity and positive predictive values when breast and prostate are the target sites. Studies on asymptomatic populations should yield sensitivity, specificity and positive predictive values when ovarian cancer is the target site.
10. As more women seek mammographic breast screening, the importance of efficient, high speed, "intelligent" mammographic systems capable of acquiring and storing large volumes of images and enhancing image interpretation will become more important. Technological developments of interest are:
  - a. Develop digital mammographic systems for high volume applications with electronic archiving and image analysis capabilities.
  - b. Develop artificial intelligence based interactive image analysis software to enhance mammographic sensitivity and specificity.

## **Other Research Topics Within the Mission of Institute**

For additional information on research topics, contact:

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### ***Division of Cancer Control and Population Sciences***

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For additional NCI-related SBIR Information, contact:

<http://www.cancer.gov/smallbusiness>

**NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)**

The NICHD conducts and supports research and research training on biological and behavioral aspects of human development. Primary program areas include: reproduction and population studies, pregnancy, perinatal biology, maternal and infant well-being, developmental and reproductive immunology, congenital defects, developmental biology, nutrition and growth, human learning and behavior, learning disabilities, cognitive and social development, mental retardation and developmental disabilities, AIDS and HIV, and medical rehabilitation.

For additional information about areas of interest to the NICHD, please visit our home page at <http://www.nichd.nih.gov>.

**Population Research**

Research on topics in reproductive sciences, contraceptive development, and demographic and behavioral sciences. Examples of research topics that may be of interest to small businesses include, but are not limited to:

- A. *Reproductive Sciences*. Research on the reproductive processes of men and women and of animals with similar reproductive systems related to developing safer and more effective means of regulating, preserving or achieving fertility. Particular areas of programmatic interest relative to small business initiatives include, but are not limited to:
1. Development of reagents to facilitate study of reproductive and developmental processes.
  2. Establishment and validation of functional cell lines.
  3. Development of novel assays, kits and devices to monitor fertility.

4. Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
5. Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.

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B. Contraceptive and Reproductive Health Research. Emphasis is on developing new and improved methods of fertility regulation, for men and for women, that are safe, effective, inexpensive, reversible, and acceptable; developing new and improved treatments for disorders of the male and female reproductive system, including those used for hormone therapy; discovery and dissemination of new knowledge concerning the medical benefits and risks of contraceptives and other drugs, devices, and surgical procedures as they affect reproductive health, primarily focusing on applied research involving epidemiology studies or Phase III/IV trials designed to detect clinically significant adverse effects, particularly those too rare to be determined through the premarketing approval process of the Food and Drug Administration. Laboratory models are utilized to further the understanding of mechanisms of action and to supplement epidemiologic and clinical observations; they are also used when human studies are not feasible. Areas of interest may include but are not limited to:

1. Developing new and improved methods of fertility regulation, for men and for women, that are safe, effective, inexpensive, reversible, and acceptable.
2. Developing new and improved treatments for disorders of the male and female reproductive system, including those used for hormone therapy.
3. The discovery and dissemination of new knowledge concerning the medical benefits and risks of contraceptives and other drugs, devices, and surgical

procedures as they affect reproductive health, primarily focusing on applied research involving epidemiology studies or Phase III/IV trials designed to detect clinically significant adverse effects, particularly those too rare to be determined through the premarketing approval process of the Food and Drug Administration. Laboratory models are utilized to further the understanding of mechanisms of action and to supplement epidemiologic and clinical observations; they are also used when human studies are not feasible.

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C. Demographic and Behavioral Sciences. Research on the size, growth, and composition of populations and the impact of changes in population on the health and well-being of individuals, families, and the population itself. The program emphasizes not only factors affecting fertility, mortality, population movement and compositional change, but also teenage childbearing, AIDS, single-parent families, racial and ethnic differentials in infant mortality, legal, and undocumented immigration, and the well-being of children. Applications are encouraged in three areas:

1. Innovative use of geographical information systems and spatial network analysis.
2. Innovative approaches to analyzing and disseminating large-scale data sets.
3. Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, and other mission-related topics.
4. Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.

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## Research for Mothers and Children

Research in seven major program areas: pregnancy and perinatology; developmental biology, genetics and teratology; endocrinology, nutrition, and growth; mental retardation and developmental disabilities; learning disabilities; cognitive and social development; and pediatric, adolescent, and maternal AIDS. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

- A. *Pregnancy and Perinatology*. Research on the physiology of pregnancy and labor; high-risk pregnancies, including those with hypertensive disorders, diabetes or seizure disorders; fetal pathophysiology; premature labor and birth; disorders of the newborn; sudden infant death syndrome; and biological and behavioral antecedents of low birth weight.

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- B. *Developmental Biology, Genetics, and Teratology*. Cellular, molecular, and genetic aspects of embryonic and fetal development and its aberrations, including early embryogenesis, limb formation, development of the nervous system, developmental and reproductive immunology, and teratology.

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- C. *Endocrinology, Nutrition, and Growth*. Research on the nutritional needs of pregnant women and their fetuses; aspects of nutrients related to reproduction, growth and development; breast feeding and lactation; the immunology of breast milk; development of the gastrointestinal system; childhood obesity and the nutritional antecedents of adult disease; developmental endocrinology; and mechanism of hormone action during growth and development.

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- D. *Mental Retardation and Developmental Disabilities*. Biomedical research in neuroscience, genetics, biochemistry,

molecular biology, and psychobiology aimed at identifying factors that cause abnormal brain maturation and function; identification of direct and indirect social, economic and cultural influences on the occurrence of mental retardation and developmental disabilities (MRDD); and research leading to the assessment, prevention, and amelioration of MRDD, including screening and prenatal diagnosis.

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- E. *Child Development and Behavior*. Research and research training programs in developmental psychology (cognitive, affective, and social development), cognitive psychology, cognitive neuroscience, language acquisition and bilingualism, developmental neuropsychology, and educational psychology; studies to define, classify, and map the developmental course of specific learning disabilities and disorders of attention; studies to elucidate the etiological role of cognitive, linguistic, perceptual, educational, genetic, social, and neurobiological mechanisms in dyslexia, learning disabilities, language disorders, and disorders of attention; investigations of the effects of well-defined treatment interventions on specific types of learning disabilities; studies designed to understand the development of attention, reasoning, planning, problem solving, and concept formation in children; studies delineating the effects of motivation, emotion, societal, cultural, familial, and neurobiological influences on social, emotional, and cognitive development; examinations of the effects of parental and non-parental care on social, emotional, and cognitive developmental outcomes; and investigations of temperament, motivation, self-concept, attitudes, and values, and their relationship to development.

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- F. *Pediatric, Adolescent, and Maternal AIDS*. Research on all aspects of HIV (human immunodeficiency virus) infection and disease, including AIDS in women of child-bearing age, pregnant women, mothers,

fetuses, infants, children, and adolescents. Areas of interest include, but are not limited to, epidemiology, natural history, pathogenesis, treatment, and prevention.

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### **Medical Rehabilitation Research**

Research is encouraged on the restoration, replacement, or enhancement of functioning required by children or adults with physical disabilities to be effective in daily life. . Emphasis is on improving functional mobility, promoting behavioral adaptation to functional losses, assessing the efficacy and outcomes of medical rehabilitation therapies and practices; developing improved assistive technology; understanding whole body system responses to physical impairments and functional changes; developing more precise methods to measure impairments, disabilities, and societal limitations; and training health professionals in the field of medical rehabilitation. The mission of the NCMRR is to increase the effectiveness of medical rehabilitation practices through research on:

- A. Improving functional mobility.
- B. Promoting behavioral adaptation to functional losses.
- C. Assessing the efficacy and outcomes of medical rehabilitation therapies and practices.
- D. Developing improved assistive technology.
- E. Understanding whole body system responses to physical impairments and functional changes.
- F. Developing more precise methods to measure impairments, disabilities, and societal limitations.
- G. Training health professionals in the field of medical rehabilitation.

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### **Other Research Topic(s) Within Mission of Institute**

For additional information on research topics, contact:

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For administrative and business management questions, contact:

Ms. Diane Watson  
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### **NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)**

The mission of the NIDA is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy. For additional information about areas of interest to the NIDA, please visit our home page at <http://www.nida.nih.gov/>.

### **Division of Treatment Research and Development**

The NIDA DTR&D supports research aimed at the development and testing of pharmacological and behavioral treatments for drug abuse and addiction. This includes the identification, evaluation, development, approvability, and efficacy testing of new and improved pharmacotherapeutic agents, as well as the testing of marketed medications, and of behavioral treatments used alone or integrated with medications. The DTR&D also advances a human neuroscience research and training program focused on understanding the neurobiological substrates of drug abuse and addiction processes.

- A. Chemistry and Pharmaceuticals Branch (CPB). The CPB supports research in the design (including molecular modeling and

structure-activity relationship studies) and synthesis of novel compounds, formulation development, bioanalytical methods development, and pharmacokinetics/pharmacodynamics aimed at the discovery and development of new medications for treating drug addiction. (NIDA-CPB). Areas that may be of interest to small businesses include, but are not limited to:

1. ***Research Related to the Design and Development of New Compounds and Improved Drug Products (Drug Delivery) for the Treatment of Drug Addiction***

- a. Synthesis of new chemical compounds that would have potential as treatment agents for the medical management of stimulant (e.g., cocaine, methamphetamine, or nicotine) addiction. Consideration should be given to the design of partial agonists or pure antagonists that diminish the reinforcing effects of stimulants, as well as full agonists that could function to normalize physiological activity following discontinuation of stimulant use. Although typically these types of compounds are designed to affect dopaminergic and/or serotonergic activity, compounds acting through other mechanisms are also of interest.
- b. The development of combinatorial libraries for discovery of drug addiction pharmacotherapies.

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- c. Synthesis of new chemical compounds with potential for the treatment of opioid dependence and/or craving. Compounds which may prevent relapse to opiate use following a period of drug abstinence are of special interest.

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- d. Synthesis of new treatment compounds with minimal

transplacental (or other) properties to minimize prenatal effects on the fetuses of pregnant addicts.

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- e. Development of new approaches for the administration of potential addiction treatment drugs with poor bioavailability, such as dynorphin and other opioid peptides.
- f. Development of controlled release dosage forms for addiction treatment medications in order to maintain therapeutic drug levels for extended periods of time to alleviate compliance problems associated with addiction treatment.
- g. Development of new approaches or improved dosage forms for the administration of addiction treatment drugs to infants suffering adverse effects due to prenatal drug exposure (e.g., opiate withdrawal symptoms).

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B. ***Medications Discovery and Toxicology Branch (MDTB)***. The MDTB supports research on the development of preclinical behavioral models (e.g., of craving, drug-seeking behavior, dependence, or relapse), biochemical assays, gene expression assays and electrophysiological methods to identify and characterize new medications to treat substance abuse, as well as pharmacological screening of novel compounds to identify potential drug abuse medications. The Branch also supports research on toxicity studies of potential medications for the treatment of substance abuse, and interactions of potential treatment medications with abused substances. Areas that may be of interest to small businesses include, but are not limited to:

- 1. ***Development of New Methods for Discovery of Medications Useful in Treating Drug Addiction***. Of special interest would be the development of

new animal models of addiction, incorporating established drug self-administration techniques that show increased relevance to the clinical setting. Development of relevant biochemical or electrophysiological screening methods is also encouraged.

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2. ***Development of Methods to Detect Adverse Cardiovascular Interactions Between Cocaine and Potential Cocaine Dependence Treatment Medications.*** The development and validation of in vitro and/or in vivo bioassay methods for the identification of adverse cardiovascular properties of potential cocaine addiction treatment medications are of special interest to the NIDA Treatment Research and Development Division. Since it is reasonable to believe that patients receiving cocaine dependence treatment medications may occasionally self-administer large quantities of cocaine, the bioassay procedures should be applicable not only to the study of the medication alone, but also to the study of cocaine/medication combinations.

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- C. ***Behavioral Treatment Development Branch (BTDB).*** The BTDB supports research on behavioral treatments and combined behavioral and pharmacological treatments. Behavioral treatments include psychotherapies, behavior therapies, family therapies, group therapies, counseling strategies, rehabilitative techniques, brief behavioral interventions, therapeutic community treatments, and other psychosocial treatments. Research on these treatments may be carried out in any setting, including both academic and community or “real-world” settings. Areas that may be of interest to small businesses include, but are not limited to:
  1. ***Behavioral Strategies for Increasing Compliance in Taking Treatment Medication.*** Research to develop and

to evaluate strategies to induce recovering addicts to take medication for a prolonged time, especially antagonists such as Naltrexone; to induce HIV infected drug users to comply with medical treatments (HAART) in drug abuse treatment settings; or to adapt existing behavioral strategies to increase patient compliance and cooperation in long-term treatment for drug abuse or for diseases associated with drug abuse such as tuberculosis or hepatitis. An important consideration should be cost and practicality of use in actual clinical practice or in an aftercare program. The product of such research might be a manual, which describes the behavioral strategy, and its implementation by treatment staff or scientific data regarding evaluation.

2. ***Integration of Behavioral Therapies and Pharmacotherapies.*** Development and testing of integrated therapeutic approaches for individuals who abuse various drugs, including methamphetamine, cocaine, nicotine, and opioids; in addition this may include individuals with co-occurring substance abuse and mental disorders, since effective treatment of both disorders may lead to improved treatment outcomes. Integrated behavioral therapies and pharmacotherapies may enhance the efficacy of both types of therapeutic interventions. For instance, the maintenance and detoxification of heroin addicts could perhaps be optimized by the integration of distinctive behavioral therapies devised specifically for opioid agonists, antagonists or partial agonists determined by the heterogeneity of the subgroup of addicts and the pharmacological differences of the medications. Integration of medications and behavioral therapies could possibly enhance compliance with medication regimens, increase retention allowing pharmacological effects to occur and prevent relapse to drug abuse and addiction.
3. ***Drug Abuse Treatment in Primary Care Settings.*** Development and testing of brief behavioral interventions

for drug use/abuse and other health risk behaviors in various populations (e.g., children, preadolescents, adolescents, women, minorities) that are seen in office-based practice and other health care settings. The brief intervention strategies may be used by a variety of health care professionals in primary health care settings. Also, development and testing of valid and reliable screening and assessment instruments to detect drug abuse that could be used by health professionals in primary health care settings.

4. ***Woman and Gender Differences in the Provision of Behavioral Treatments, and HIV/AIDS Risk Reduction Approaches.***

Develop and evaluate specific behavioral treatment approaches targeting drug-addicted women. This may include behavioral therapies, skills training techniques, counseling strategies, and HIV and other infectious disease behavioral risk reduction strategies. . This may also include development and testing of training materials that specifically address women and gender differences in drug addiction treatment to promote effective use of research-based treatment approaches. Training materials may involve treatment manuals, training videos, CD and CD ROM technology or other innovative educational strategies for health professionals.

5. ***Transporting Behavioral Treatments to Community Practitioners.***

There is a need for effective methods of transferring behavioral therapies found to be effective in clinical trials to clinical practice. Cognitive-behavioral therapy, operant behavioral therapy, and family therapy are among the therapies that have been shown to be efficacious in a highly controlled setting and may be helpful treatment approaches in community treatment programs as well. However, community practitioners may have been trained using other approaches and may not have been exposed to these scientifically-based approaches. This is a call for proposals that examine mechanisms to transfer effective research-based drug abuse treatment information and skills-based

techniques to practitioners in the community. This may involve the development and testing of training materials and procedures to use in the training of community practitioners to skillfully administer these treatments, including the development of highly innovative technology transfer and communication approaches. Research testing the transportability of empirically supported therapies to the community (Stage 3 research) is an important component of the Behavioral Therapies Development Program.

There is also a need for the development of educational methods to train non-drug abuse health care workers in relating to drug abusers; eliciting medical histories regarding past or present drug abuse; recognition of the signs and symptoms of drug abuse; identification of those at high-risk for HIV and other drug abuse related medical problems such as tuberculosis or hepatitis. Development and validation of a drug abuse screening instrument which can be administered by primary health care providers, and training in administering such an instrument.

6. ***Using Telemedicine to Disseminate Drug Addiction Research Findings to Primary Health Care Providers.***

Telemedicine programs are being used in urban medical centers to rapidly disseminate science-based information on new medical treatments. In addition, approximately one-third of the rural hospitals are now using telemedicine to improve patient care. Health care professionals need science-based information on drug abuse prevention and treatment. Research to develop and evaluate telemedicine programs to transport science-based information on drug addiction to the primary health care community is encouraged.

7. ***Developing Culturally Sensitive Behavioral Therapies for Racial and Ethnic Minorities.***

Minority populations are disproportionately affected by the consequences of drug abuse. Research to develop and evaluate behavioral treatments that are

culturally sensitive and relevant for diverse racial and ethnic minority populations is encouraged. This may include studies of behavioral treatments, alone or in combination with pharmacological treatment, or studies of behavioral strategies for increasing adherence to taking medications. In the development and evaluation of the behavioral treatment, attention needs to be directed at examining medical, social, and cultural factors that may influence adherence to the behavioral treatment approach and treatment outcome.

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8. ***Behavioral Therapy Development.***

Development of new or refinement of existing psychotherapies, behavioral therapies, skills training techniques or drug counseling strategies for the treatment of drug abusers/addicts. Incorporation of HIV risk reduction strategies as an integral component in routine counseling or other behavioral interventions. This would include the development of: therapy manuals, to define exactly what the therapy is and how to administer it optimally; competence and adherence scales, to evaluate the extent to which therapists and counselors are actually providing the therapy intended; process measures, to measure various aspects of the therapeutic interaction; and measures of the integrity and fidelity of the therapy. The following are of particular interest:

- a. Development of behavioral therapies or components of such therapies that are based on developments and findings from the basic behavioral or cognitive sciences.
- b. Discrete therapy components that address specific problems common among drug addicted individuals and that can be implemented in conjunction with other therapeutic services. For example, an investigator may wish to develop a four session, highly focused, job

seeking skills module that can be easily implemented by a wide range of practitioners to effectively increase appropriate job seeking behavior. Other examples include, but are not limited to, modules to engage ambivalent drug dependent individuals in treatment, modules to increase assertiveness in female drug addicts who feel pressured by others to use drugs, or to incorporate effective HIV risk reduction techniques.

- c. Therapies designed specifically to engage and retain individuals in treatment, especially those at high risk for HIV. An example could be a therapy that is: (1) sensitive to the motivational level of the client; (2) is specifically designed to respond to the needs of the individual, whatever his or her motivational level might be; and (3) actively works to increase an individual's desire to remain in treatment.

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9. ***Innovative Technologies for Drug Abuse Treatment and HIV Risk Reduction.***

Research directed at the development and evaluation of innovative technologies to treat substance abuse and/or reduce risk for HIV infection. Approaches should be capable of being readily incorporated at reasonable cost into various treatment settings. Areas of interest include CD-ROM technology, audio delivery devices, photo therapeutic instruments, and virtual reality devices.

10. ***Development of HIV Risk Reduction Intervention.***

Research to develop and evaluate behavioral strategies to reduce HIV risk behaviors in HIV-positive and HIV-negative substance abusing treatment populations. AIDS prevention programs should emphasize risk education, sexual assertiveness, skills training in condom use, problem solving skills, self-management of risky situations, and peer support for change efforts. Risk reduction interventions for HIV-infected patients should be

specially adapted to their potential cognitive impairments and should address compliance with medical regimens and their unique emotional needs. The product of such research might be educational materials such as manuals or videotapes that describes the intervention and its implementation by treatment staff.

11. ***Alternative and/or Complementary (A/C) Interventions for Drug Abuse Treatment.*** Research is encouraged on alternative or complementary interventions for drug abuse treatment, A/C interventions could be the sole treatment or could be adjunctive strategies to enhance the therapeutic potency of existing drug abuse treatments. An example of an adjunctive A/C intervention might be where the A/C intervention reduces withdrawal symptoms thus enhancing retention in treatment. Included would be interventions that are commonly used in “real world” treatment settings, but whose therapeutic efficacy has not been scientifically demonstrated. Such interventions include acupuncture, bioelectrical stimulation, exercise, biofeedback, meditation, among others. The product of this research might be a manual or video, which illustrates the intervention and how it is implemented by treatment staff.

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12. ***Development of New or Improved Addiction Assessment Measures and Procedures.*** Research directed at the improvement of a currently available measure or the design of a new psychosocial, social or environmental measure appropriate for use in the clinical assessment of substance abusing populations. Special consideration should be given to a specific screening or diagnostic tool, or to a specific measure of treatment readiness, treatment compliance, service utilization, therapeutic process or drug treatment outcome. The scope of the study might cover the establishment of the instrument's

reliability (e.g., inter-rater; test-retest; item-analysis), validity (e.g., discriminant; construct; concurrent; predictive), sensitivity/ specificity, a normative data set for a specific clinical population, a standardized form of administration, different response formats, a specific language version other than English, and/or the instrument's utility in different clinical settings.

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13. ***Behavioral Therapies for Pre-Adolescents and Adolescents.*** Behavioral therapies for pre-adolescents and adolescents that incorporate HIV risk reduction counseling as an integral component of the treatment. This includes the development of new, or refinement of existing psychotherapies, behavioral therapies, and counseling (group and or/individual). This also includes the development and testing of manuals as well as other creative, interactive approaches for therapy delivery that may consider different settings for delivery, such as primary care, school-based health programs, juvenile justice settings, etc. Also the behavioral treatments should be culturally and gender sensitive.

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#### D. *Clinical Neurobiology Branch (CNB)*

The CNB supports research on the clinical neurobiology of addiction (exploring alterations of the structure and/or function of the human central nervous system following acute or chronic exposure of drugs of abuse), and the neurobiology of development (neurobiological effects of drugs of abuse and addiction during various stages of development and maturation, effects of drug exposure on neurobiological processes, development of methodologies and refinement of techniques used in pediatric neuroimaging). The Branch also supports cognitive neuroscience of drug abuse and addiction,

and the neurobiology of treatment, HIV/AIDS, and human pain and analgesia. Areas that may be of interest to small businesses include, but are not limited to:

1. ***Development of Novel Approaches in Human Neuroscience***

- a. Development of innovative, noninvasive research methods or novel approaches to identify various neurobiological markers of brain alterations in humans induced by acute or chronic exposure drugs of abuse. This may include the identification of neurobiological (including genetic) markers that might be associated with risk for, or resilience to drug abuse and addiction. Of particular interest are noninvasive methods that could be used to determine the effects of drug abuse/addiction treatments on neurobiological systems in an attempt to understand the neurobiological processes underlying therapeutic efficacy.
- b. In recent years, there has been an increase in studies employing functional magnetic resonance imaging (fMRI) to understand brain processes and functional neuronal systems. In particular, these neuroimaging techniques are being used to probe how drugs of abuse alter brain functioning. Consequently, there is a need for the development of stimulus generation hardware to be used in an fMRI scanner that can display stimuli important in drug studies. As the studies of brain function become more sophisticated, task-related assessments of brain activation are increasingly important. Shielded goggles or other types of visual stimulation hardware is necessary for presentation, for example, of neurocognitive tasks, drug-related images for the induction of craving, or other "virtual reality" types of dynamic stimuli important in studies of drug abuse and addiction. Responses to this type of stimulation then could be

correlated with brain measures using neuroimaging techniques. These types of studies will provide new insights into drug-brain-behavior interactions.

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- c. Virtual Reality for the Neurobiological Study of Drug-Brain-Behavior Interactions and Drug Abuse Treatment. Virtual Reality (VR) is an emerging technology proven useful throughout Europe and America in a variety of research-related, therapeutic and instructional settings. By immersing a person's senses in a synthetic world or Virtual Environment (VE) that characterizes VR, a highly flexible and programmable set of stimuli can be used to enhance the standard approaches used in neuropsychological assessment. Collection of real time data and bulk data recording can provide a correlation of a stimulus reference signal with simultaneously collected fMRI scanner and physiological data over time. Unlike most computer access systems that accept only one or two modes of precise and/or discrete input at a time, VR systems have the potential to monitor movement or action from any, or many, neurobiological functions at once. In addition, the multimodal feedback inherent in VR provides a way to vary nonvisual stimulus components (e.g., resistance, temperature, pitch) in a way that is impossible to achieve via standard computer systems. Finally, VR systems provide a bypass for keyboard entry or direct manipulation environments (e.g., pointing instruments like the mouse), by allowing the manipulation of multi-sensory representations of entire environments by natural actions and gestures.

The applications of VR in clinical and basic neurobiological research are uncovering many findings of interest. For example, Ghahramani and Wolpert (1997) used VR to investigate modular decomposition in visuomotor learning with results suggesting that the brain does employ a decomposition strategy during learning. fMRI and VR have been used by Aguirre, Detre, Alsop and D'Esposito (1996) to localize the neural substrates of human topographical spatial learning within the hippocampal system to address conflicting evidence on the regional function of the medial temporal lobes in rodents and primates. Neuronal responses in the motion pathway to natural optic flow stimuli were examined in a macaque monkey (Pekele, Lappe, Bremmer, Thiele, and Hoffmann (1996). There are VR systems that have been specifically designed for the assessment of cognitive functions in individuals with acquired brain injuries. In one instance, VR produced objective clinical evidence of a persisting frontal dysfunction in spite of normal neuropsychological tests traditionally used to tap frontal function.

VE can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction. For example, VR affords one an avenue to present of a variety of complex, multi-sensory stimuli for neurocognitive tasks or, alternatively, the dynamic stimuli important for producing drug-related images for the induction of craving. VR can also be tested as an alternative to traditional behavioral therapies in the treatment of drug abuse. Responses obtained as a result of the above can then be correlated with brain measures using state-of-the-art neuroimaging techniques. We, therefore, invite studies employing VR, especially to probe

brain processes in drug abuse/addiction combined with neuroimaging methods (contact Ro Nemeth-Coslett), or to be developed or applied as a potential treatment for substance abuse (contact Debra Grossman).

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- d. Development of interactive computer applications for neuropsychological/ neurocognitive assessment to determine functional brain deficits in acute and chronic drug abusers. In addition, a neurobehavioral test battery to assess other neurobehavioral/ neurocognitive deficits resulting from drug abuse/addiction is encouraged. Of particular interest is the development of such assessments for use in children and adolescents exposed to drugs of abuse to better define and understand the effects of early exposure on brain function and development.

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E. Medications Research Grants Branch (MRGB)

The MRGB supports research on controlled clinical pharmacological studies to assess a compound's potential as a drug abuse treatment medications, controlled clinical trials for the development or new agents for treatment, or complications of drug abuse (withdrawal, relapse, overdose).

**Division of Basic Neuroscience and Behavioral Research (DNBR)**

DNBR's basic neuroscience and behavioral research focuses on understanding the mechanisms, characteristics, and processes of drug abuse. Basic behavioral, cognitive, neurobiological, cellular, molecular, chemical, and genetics research aims at characterizing

and understanding drug seeking, compulsive behavior, and addictive processes. These research areas necessarily include studies of normal processes.

Using both animal and human studies, basic behavioral research focuses on behavioral and cognitive processes that may or do lead to drug initiation, and the behavioral and cognitive consequences of drug abuse. Neurobiology research focuses on the neural mechanisms and substrates underlying behavioral and cognitive processes and vulnerability factors associated with drug abuse, addiction, sensitization, tolerance, and relapse.

DNBR supports basic chemistry and pharmacological studies focusing on structure/activity relationships, definition, and characterization of systems involved in drug actions, chemical synthesis of new ligands, pharmacokinetics, analytical methods, understanding basic mechanisms of drug action and drug testing.

Computational and theoretical modeling of biological systems and behavioral processes, biomedical computing and/or information science and technology development is supported by DNBR.

1. ***Research Related to the Design of New Therapeutic Approaches.***

Development of new therapeutic approaches based on the application of nanoscale particle formulations for drugs that are either poorly water-soluble or otherwise unstable under physiological conditions, and development of methods for using nanoscale formulations for targeting specific brain sites or to control drug delivery over extended periods of time.

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2. ***Virtual Reality for Treatment of Pain.***

Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) exposure can reduce reported pain during wound care. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of pain. Development of treatments for both acute and chronic pain are sought. These treatments can be based in clinical

settings or the patient's homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.

3. ***Virtual Reality for the Treatment of Drug Abuse.***

Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to ignore drugs cravings, withdrawal symptoms or environmental cues that promote drug abuse. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of drug abuse. These treatments can be based in clinical settings or the patient's homes. These treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies to address abuse of all types of drugs (e.g. cocaine, marijuana, nicotine, alcohol, inhalants) are sought. Phase I testing should establish the feasibility of the use of this technology for the particular drug problem addressed (e.g. cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should involve larger-scale testing (e.g. more subjects and treatment trials) examining various treatment parameters (e.g. timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

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4. ***Development of innovative probes and research products/dosage forms for drug abuse/addiction research.***

Proposals are solicited for the synthesis of or development of chemicals/drug products/metabolites (agonists, and/or antagonists), or new probes for drug abuse research that can easily be made available to the drug abuse research community at a much reduced cost as compared to current commercial prices. Such compounds could be of any category - narcotics, stimulants, sedatives, or cannabinoids; drug metabolites and drug products.

Proposals are encouraged that describe methods that:

- a. Improve the purity of the compounds;
- b. Alter the delivery characteristics of drug products; and
- c. Propose new chemicals/drug products that are in demand by drug abuse researchers, but are not available currently or are available with great difficulty. The proposal should specify the drug/drug product to be produced.

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5. ***Chemical Libraries for Drug Development.*** The development and biological screening of lead compounds and their combinatorial libraries for use in the area of drug abuse treatment research are encouraged, such as generation of new ligands having opiate receptor selectivity, or ligands with NMDA or serotonergic agonist/antagonist activity and/or related. These are designed as lead compounds either for drug design or as tools to elucidate mechanisms of action of drug abuse.

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6. ***Analytical Techniques.*** The development of new analytical methods or reagents for use in measuring drugs of abuse and their metabolites in biological

systems, such as urine, blood, saliva, sweat, hair, breast milk, brain tissue, and meconium. The methods should be efficient, sensitive, convenient, and cost effective. Modifications and improvements in existing analytical techniques would also be considered, particularly those improving sensitivity and selectivity.

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7. ***Conantokins.*** Research SBIR/STTR applications are sought in which naturally occurring conantokin neuropeptides G, T, and R are modified by the use of combinatorial synthesis or by amino acid replacement/addition(s), to provide new ligands having potential antagonistic activity at one or more NMDA binding sites. These agents are of interest for the reduction of acute or chronic pain, when used as single agents, or in combination with opioids such as morphine. Their ability to attenuate the development of morphine tolerance is also considered a critical aim. The testing of such compounds should also serve to better define their in-vitro pharmacological action in terms of competitive versus non-competitive inhibition, their particular binding site(s), and their NMDA subtype selectivity. The testing should also include their in-vivo activity in animal models of acute, chronic, and neuropathic pain.

Phase I and Phase I/Phase II Fast Track applications will be considered.

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8. ***Genetic Studies.*** The National Institute on Drug Abuse is interested in SBIR proposals that would greatly facilitate the identification of genetic loci that confer vulnerability to substance abuse and addiction. Areas of interest include but are not limited to:

- a. Collection and genotyping of human pedigrees and sib-pairs for vulnerability or resistance to drug abuse.
- b. Isolation and identification of mutant strains in genetic model systems such as Zebrafish, *Drosophila*, *C. elegans*,

mice, and rats that are more vulnerable or resistant to drugs of abuse.

- c. Design, development, and marketing of behavioral apparatuses to conduct rapid behavioral throughput screens for identifying genetic vulnerability to addiction in genetic model systems.
- d. Development of transgenic models for drug abuse using bacterial artificial or yeast artificial chromosomes.
- e. Development of software and databases for candidate genes for drug abuse.
- f. Identification and mapping of functional polymorphisms of candidate genes for drug abuse.
- g. Placement of candidate genes for drug abuse on biochips.
- h. Marker-assisted breeding of congenic mouse and rat strains for mapping quantitative trait loci associated with addiction and drug abuse.
- i. Vectors for gene transfer into neurons.

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9. ***Drug Testing Development.***

Development of new, more refined or more practical drug testing methodologies. Studies may focus, but are not limited to the following topics: drug testing methods; drug extraction procedures; methods to control for possible environmental contamination factors; and reference materials. Methodologies with special application to the workplace, the emergency room, the transportation environment, or other specific settings are welcome. Methodologies with an emphasis upon circumstances for testing such as post-accident testing or readiness for work testing are also encouraged.

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10. ***Biotechnology.*** Development and improvement of techniques for the crystallization of membrane channel proteins usable for structural (microscopic and 2D crystallographic) and functional

studies. Applications may focus on various aspects of protein purification, solubilization, and reconstitution in lipid monolayers or bilayers, and crystallization.

The goal of the work could be commercialization of a process, reagent, or final product. Application of these techniques to nicotinic acetylcholine receptor subtypes and the NMDA subtype of glutamate receptors would be of particular interest to this Institute.

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11. ***Effects of Drugs at the Cellular Level.***

Development of new imaging techniques, reagents and related hardware and software for dynamic investigations of the effects of drugs of abuse on cellular activities and communications. For example, these techniques might include, but are not limited to, development and utilization of reagents for magnetic resonance microscopy and other MRI methods; development of methodologies applying functional MRI to drug abuse studies; the use of dyes, intrinsic signals, and other optical indicators for studying signal transduction mechanisms, the regulatory control of protein entities (such as phosphorylation), and neuronal excitatory and inhibitory pathways. Areas of interest may include, but are not limited to:

- a. Studies using molecular biological techniques to scale-up protein production for investigations aimed at enhancing understanding of the structure, function and regulation of molecular entities involved in the cellular mechanisms through which abused drugs act.
- b. Validated in vitro test systems can reduce the use of animals in screening new compounds that may be of potential benefit in treating drug abuse. Test systems are needed to evaluate activity at receptors or other sites of action, explore mechanism(s) of action, and assess potential toxicity.
- c. With the recent success in molecular cloning of various drug abuse relevant receptors, enzymes, and other proteins, researchers will elucidate the molecular mechanism of action of

these drugs. Studies to generate strains of transgenic animals carrying a gene of interest are solicited. Of special interest are knockout and tissue-specific knockout animals. These animals can be used to identify gene function, and to study the pharmacological, physiological, and behavioral role of a single gene.

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## 12. **Toxicity Studies**

- a. Studies on abused drugs and their metabolites to develop methodologies that may be potentially useful in addressing medical emergencies. Such studies might include investigations involving development of pharmacokinetic models, methodologies, and data.
- b. Concern remains about the potential acute and chronic neurotoxicity of drugs of abuse. Information is needed about the possible neurotoxicity of pharmacotherapeutic agents with potential for treating drug abuse. Improved methods are needed for identifying, assessing, and quantifying the nature and extent of neurotoxicity. Such studies might include the development or application of quantitative chemical, physiological, or behavioral measurements relating to nervous system injury or methods for quantitative analysis of damage.

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13. **Development of Diagnostic Tools that are Predictive of Cardiovascular Complications Associated with Crack/Cocaine Use.** Studies of cardiovascular function are important because of the cardiac complications associated with crack/cocaine use. The mechanisms involved are poorly understood yet, in many cases, life threatening cardiac and vascular events associated with cocaine use have occurred in young healthy individuals. Experimental findings indicate that there may be a sub-population of animals that are more

sensitive to cardiotoxic effects of cocaine. Studies are needed to better understand the cardiovascular effects of cocaine in humans.

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14. **Predisposition to Cardiovascular Complications Associated with Abused Substance(s).** Development of experimental animal models to assess a genetic predisposition or increased sensitivity to cardiac and vascular complications associated with drug use. Such studies might include, but are not limited to, investigations involved with biochemical, physiological and pathological indices of cardiovascular system function.

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15. **Opioid Peptides.** Research and development directed at the medicinal chemistry and molecular pharmacology of opioid peptides, especially in methods development. Areas of interest include but are not limited to:
  - a. Development of innovative methodologies for the synthesis of opioid peptides to be made available to researchers. Syntheses proposed should be limited to single analogs.
  - b. Methods to identify new ligands for opioid receptors and the design of new opioid peptide analogs with therapeutic potential.
  - c. Development of analytical methodologies for the quantitation of synthetic and endogenous opioid peptides, peptide precursors, and processing enzymes. The innovation may be limited to a part of the method, such as development of a special detector or a sample cell. Methods might include antibody development and development of innovative immunoassays.

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16. **Dopamine and Serotonin Receptor Ligands.** Both dopamine and serotonin receptors exhibit multiple subtypes. Applications are solicited using chemical combinatorial library techniques to develop ligands having a high degree of selectivity to these receptor subtypes, which can be useful both as pharmacological tools and lead compounds in medicinal chemistry/drug development.

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#### **Office of Science Policy and Communications (OSPC)**

##### **A. Science Policy Branch (SPB)**

1. **Science Education.** In order to improve science education in the area of drug abuse research (e.g., disciplines such as neuroscience, psychology, epidemiology), efforts are needed to develop innovative methods for improving knowledge of and generating interest in science among school children, the general public, and health care providers, including providers involved in drug abuse treatment. These might include but are not limited to:
  - a. Development of methodology to present drug abuse and science information to particular groups, such as kindergarten and elementary school students, African Americans, Hispanics, persons with disabilities and health care providers.
  - b. Development of methodology to transfer new knowledge and directions of scientific growth to teachers, curriculum developers and health care providers.
  - c. Development of computer based learning systems that allow students to experience the scientific process.
  - d. Development of specific materials, activities, or programs that promote science education related to drug abuse, such as exhibits, curriculum materials, coloring books, videos,

teacher education workshops, partnership programs with scientists and educators, or workshops for health care providers.

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#### **Division of Epidemiology, Services and Prevention Research (DESPR)**

##### **A. Prevention Research Branch (PRB)**

The Prevention Research Branch (PRB) supports a program of research in drug abuse and drug related HIV prevention to (1) examine the efficacy and effectiveness of new and innovative theory-based prevention approaches, (2) determine the components of research-based intervention strategies and programs that account for effectiveness of approaches, (3) clarify organizational, management, and delivery factors related to the effective and efficient provision of prevention services, and (4) develop and test methodologies appropriate for studying these complex aspects of prevention science. For examples of areas of interest, see NIDA-PRB.htm.

1. **Prevention Research.** Prevention research is encouraged to conduct rigorous scientific study of multiple component substance abuse prevention technologies to be implemented through multiple levels of the social environment including: the family, schools, peer groups and organizations, the workplace, health care systems, etc. The purpose of this research is to determine the efficacy and effectiveness of programming or technologies in preventing the onset of drug use and progression to abuse and addiction. Technologies should entail a comprehensive approach at the universal, selective, and/or indicated levels. Universal prevention interventions target the general public or a whole population group. Selective prevention interventions target individuals or a subgroup of the population with defined risk factors for substance abuse. Indicated preventive interventions target individuals or

subgroups who are identified as having detectable signs or symptoms foreshadowing drug abuse and addiction and who have not met diagnostic criteria. NIDA encourages the development and testing of innovative prevention intervention technologies that are sensitive and relevant to cultural and gender differences. These technologies may include, but need not be limited to, the Internet, CD-ROM programs, test materials and videos, as well as tele-training via satellite, computer-assisted instruction, and virtual reality. Specific areas of interest include, but are not limited to:

- a. Methodological research in the field of drug abuse prevention on promising data collection, analyses and reporting techniques that are sensitive and relevant to cultural and gender differences.
- b. Studies that assess reliability and validity of self-report, physiological, and biochemical measures for use in prevention trials under a variety of settings.
- c. Laboratory studies of the mechanisms and effects of persuasive communication (e.g., mass media and print media) on drug related cognition, affect, motivational levels, and behaviors.
- d. Research on the development of risk profiles and assessment methodologies for identification of individuals at-risk for drug abuse.
- e. Design and testing of developmentally appropriate and psychometrically sound diagnostic instruments and observation systems for young children and preadolescents.
- f. Prevention materials and methods development for prevention service delivery in settings that are seldom utilized, i.e., health care systems, workplace, school health.
- g. Prevention services research on how drug abuse prevention programs are organized, financed, delivered, and utilized.

- h. Prevention intervention dissemination technologies, mechanisms, and links that integrate research with practice; specifically the transfer of drug abuse prevention information to practitioners, policy makers, and the public.
- i. Development of community needs assessment tools and services.
- j. Training modules for program implementors of research based substance abuse prevention programs.
- k. Strategies for integration of proven prevention approaches into existing service delivery systems.
- l. Decomposition of prevention programs to understand components that account for program effectiveness.

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#### B. Epidemiology Research Branch (ERB)

The Epidemiology Research Branch (ERB) supports an extramural program for epidemiologic research concerning drug abuse which includes (1) incidence and prevalence of drug abuse (in various stages) and related conditions such as HIV/AIDS among general and specific subpopulations, (2) identification and study of resiliency and risk factors associated with drug abuse and related conditions, (3) etiologic studies on the origins and pathways of drug use during various stages of human development, (4) methodological studies designed to measure and improve the accuracy, collection, and reporting of data on drug abuse and related conditions, (5) development of innovative statistical approaches and research designs leading toward improved analysis of drug abuse characteristics, (6) international epidemiologic studies on drug use patterns, etiologic factors, and related concerns in various national and regional contexts. For examples of areas of interest, see NIDA-ERB.htm.

#### 1. ***Assessment and Improvement of the Validity of Sensitive Data Collected***

**in Drug Use Surveys.** The accuracy and validity of self-report of drug use and related behaviors and consequences in the context of epidemiologic surveys is a matter of great concern. Research is needed on various methods of survey data collection that assures more accurate reporting. Techniques such as those based on variations in standard survey protocols, and those based on use of computer-assisted self-interview (CASI) or computer-assisted personal interview (CAPI) methods are encouraged.

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2. **Micodata Disclosure Analysis.** In the drug abuse field some data sets cannot be released for secondary analysis because of the possibility of disclosure of sensitive information about individuals and organizations. Even without individual identifiers (such as name, address, etc.), disclosure might occur through matching with administrative databases, computer-assisted searching of files to find records with particular data, or, more benignly, through researchers' presentation of summary data for categories small enough to allow inferences regarding particular individuals or organizations. For data from surveys with complex sample designs, this problem is complicated by the need to provide record-level sampling information to support appropriate data analysis. Development of (a) methods for assessing the contents of microdata files (especially longitudinal data) to determine the risk of disclosure of identifying information and (b) methods of modifying data files to substantially reduce the risk of disclosure while maintaining their usefulness for research would facilitate the availability of files for secondary analysis. Most important is the development of techniques designed to quantitatively access the amount of disclosure risk so that decisions can be made regarding

the modification or exclusion of microdata elements.

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3. **Development of Standardized Instruments for Measuring Illicit Drug Use, Abuse, and Dependence.** Accurate instruments for identifying and classifying use, abuse, and addiction of illicit substances are essential in research on the epidemiology, etiology, and consequences of these disorders and in studies of the progression from drug use to abuse and addiction. Currently, abuse and addiction of illicit drugs can be defined using a variety of diagnostic instruments; they include the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition, American Psychiatric Association, ICD 10 (International Classification of Diseases, 10th revision, World Health Organization), and others. The development of new or enhanced protocols for measuring use, abuse, and addiction should be based on state-of-the-art technology (e.g., use of computer assisted survey information collection systems) resulting in a high level of reliability, validity, and accuracy when used in a variety of survey settings (e.g., cross-sectional household surveys or retrospective cohort studies utilizing data solicited via personal visit, telephone, or mail) and population domains (e.g., general household population, children, homeless, institutionalized). The development of a culturally sensitive instrument that includes measures of risk factors associated with the initiation and continuation of drug use is particularly encouraged.

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#### C. Community Research Branch

The Community Research Branch (CRB) supports research that focuses on the epidemiology, etiology, and prevention of adverse behavioral and social

consequences associated with drug abuse which includes research to (1) identify, describe, and estimate the prevalence and incidence of adverse effects associated with drug abuse, (2) investigate the antecedents and determinants of adverse outcomes associated with drug abuse, (3) explore the role of emerging patterns of drug abuse on adverse behavioral and social outcomes (e.g., education attainment, violence, poverty) as well as the role of adverse outcomes on further drug involvement, and (4) develop, implement, and evaluate prevention interventions to mitigate or contribute to adverse consequences of drug abuse. For examples of areas of interest, see NIDA-CRB.htm.

1. ***Instrument Development for Assessing Community Factors that Affect Drug Use and its Consequences.*** Essential to the assessment and analysis of the relationship between contextual/environmental, sociocultural factors, and health is the consideration of community milieu, as the social, physical and economic characteristics of the community context can have both short- and long-term consequences for community members' physical and psychological well-being. In order to elucidate this important connection between community characteristics and behavioral and social consequences of drug use, this announcement is soliciting applications for the development of community diagnostic instruments to facilitate psychometrically sound assessment of such factors. In this context, community is defined in its broadest sense to include social groups comprised of individuals who have formed attachments based on a variety of shared factors, such as, kinship, beliefs and values, race and ethnicity, and territory (e.g. neighborhood). Instruments are needed to provide local specificity on the physical characteristics as well as the characteristics of important social groups (including the dynamic nature of individuals involvement in such social groups). Such standardized

assessments of community characteristics are needed to better understand the full impact of drug use on behavior and to develop targeted interventions to specific community needs.

The consequences of drug use and/or abuse in society take a profound toll on families, schools, and other community institutions and burden the criminal justice, health care, and social welfare systems. Consequences of interest include, but are not limited to, educational and occupational problems (illiteracy, school dropout, unemployment, job absenteeism and turnover), individual criminal activities (violence, vandalism, homicides, sexual abuse, delinquency), and poverty, homelessness, gang activities, drug trafficking and distribution systems, and family disruption and dislocation (family violence, divorce). Yet, research to enhance the understanding of how community factors affect the prevalence and incidence of such outcomes is hindered by a lack of standardized measurement instruments to aid in defining and assessing critical community factors.

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#### D. *Services Research Branch (SRB)*

The Services Research Branch (SRB) supports a program of research on the effectiveness of drug abuse treatment with a focus on the quality, cost, access to, and cost-effectiveness of care for drug abuse dependence disorders. Primary research foci include: (a) the effectiveness and cost-benefits and cost-effectiveness of drug abuse treatment, (b) factors affecting treatment access, utilization, and health and behavioral outcomes for defined populations, (c) the effects of organization, financing, and management of services on treatment outcomes, (d) drug abuse service delivery systems and models, such as continuity of care, stages of change, or service linkage and integration models, and (e) drug abuse treatment services for HIV seropositive patients and for those at risk of

infection. For examples of areas of interest, see NIDA-SRB.htm.

1. **Clinical Staff Management and Development Strategies.** This SBIR initiative will support research to design and test effective models to manage clinical drug abuse treatment staff, to systematically monitor patient problems and clinical issues, and to provide staff development to improve the quality and outcomes of care.

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2. **Drug Abuse Treatment Economic Research.** This initiative will support research to design and develop data systems for financial management and economic analysis of treatment programs and larger systems in new healthcare settings and managed care networks. Managerial decision-making requires the implementation of sophisticated data systems to facilitate routine budgeting processes, allocation of resources, performance measurement, and pricing decisions. The focus is on the needs of managers within the organization and managers outside of the organization. Data system development must be based on standard cost behavior and profit analysis. Data systems must be designed with correct cost concepts (accounting and economic) in order to permit cost and pricing decisions to be developed for new treatment technologies and management of on going systems. In research settings, such an initiative is vital for the assessment of new technologies developed for transfer to practice.

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3. **Personnel Selection Technology Research for Drug Abuse Treatment Clinics.** NIDA would be interested in supporting small innovative research that develops and validates generic selection systems that could be adopted and tailored for use by drug abuse treatment clinics. Like many

small businesses, drug abuse treatment clinics have problems attracting and retaining qualified personnel. Also like many small businesses, treatment clinics have limited resources to apply to the recruiting and hiring of new and replacement personnel. Though reliable data are lacking, a great many clinic directors complain of high annual staff turnover rates. This has been attributed anecdotally to poor quality of work life, low wages, low skill levels, incompatibilities with the clinic's treatment philosophy, and the high stress of working with drug abusers. Research has shown that the application of standardized selection methods designed to maximize person-job fit can cost-effectively reduce staff turnover. Systematic methods such as background inventories, protocol-driven interviews, aptitude tests, and credit checks have demonstrated validity for improving person-job fit. Examples of possible projects might include development of easy-to-understand guidance about legal considerations in hiring practices, software that transform job task analysis into selection criteria, interview protocols to standardize applicant screening, tolls to help improve recruitment, and/or self-paced training for hiring officials or interview panels to improve screening reliability.

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4. **Customer Retention Technology.** Premature disengagement from drug abuse treatment participation is a common problem and ranges from approximately 30 to 60% based upon the clinic and modality studied. Past research has very frequently attributed dropping out of treatment to participant characteristics (e.g., motivation, addiction severity, co-morbidity) and/or environmental factors (e.g., social pressures, unemployment, homelessness). Seldom has the dropout problem been studied in the context of customer satisfaction. That is, there is little research looking at the causes of dropping out of treatment

attributable to organizational factors (e.g., policies, practices, context) that influence participant withdrawal decisions. Needed are tools and system for assessing and survey drug abuse treatment program participant perceptions and satisfaction levels, summarizing and report participant assessments, interpreting results and adjusting policies and practices to improve satisfaction and participant retention in treatment.

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5. **Effective Management And Operation of Drug Abuse Treatment Services Delivery.**

The bulk of drug abuse treatment is conducted in small clinical settings with therapeutic staffs of less than a dozen people. Small clinics lack resources to help improve efficiency and effectiveness in both business and therapeutic practices. Areas that may be of interest to small businesses include, but are not limited to:

- a. Computer-based leader/manager self assessment tools to enable those supervising the delivery of drug abuse treatment services to gain insights about strengths and weaknesses, and to help guide them to improved leadership and management practices.
- b. Organizational change tools: Handbooks describing step-by-step way to introduce more efficient business practices such as quality management/monitoring, creating empowered work teams, formalized goal setting, improved customer relations, forming organization linkages, and adopting new fiscal and resource management techniques.
- c. Organizational change tools: Handbooks describing step-by-step ways to introduce more efficient or effective therapeutic practices such as, adding pharmacotherapy in a previously drug-free clinic, adopting new medical/pharmacotherapy or behavioral interventions, and

adopting new approaches to clinical collaboration and/or case management.

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6. **Web-Based Technologies: Transporting Services Research to Practice.** This initiative will support the development and testing of the effectiveness of web-based technologies that facilitate transporting drug abuse prevention and treatment services research to practice. Implementation of drug abuse programs in natural settings often is hampered by the lack of needed data on, first, the contents of an intervention, and second, on procedures for implementation – including, agency and/or community organizational structural and financial issues. The application may include, but is not limited to, the development of a web-based/internet-based dynamic library system that would provide current information/findings (targeted research summaries, recruited list serves and other print/electronic communication) on how to effectively and cost-effectively organize, structure and manage prevention and treatment delivery.

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**Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA)**

The Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) develops and administers a national and international program of research on HIV/AIDS and other medical/health, mental health, and developmental consequences of drug abuse. CAMCODA also coordinates research activities, and collaborates with other NIDA components, on issues concerning HIV/AIDS and consequences of drug abuse.

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1. ***Develop Improved Technology for Assessment of Prenatal Drug Exposure and Passive Postnatal Drug Exposure***

- a. Develop and refine methods for the detection and quantification of infant exposure to drugs of abuse during pregnancy, including cocaine, marijuana, opiates, and methamphetamines.
- b. Develop and refine methods for the detection and quantification of passive exposure to illicit drugs during infancy and childhood.

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2. ***Develop Interactive Database Systems on Human Subjects Issues for Use by Drug Abuse Researchers Studying School-Age Children and Adolescents Drug Use.*** Develop systems to assist investigators in obtaining technical and legal information relevant to involvement of children and adolescents in research on drug abuse. Examples of pertinent situations include tracking long-term health and development of children exposed to drugs during pregnancy, and investigating vulnerability and possible pathways to drug abuse among school-age children and adolescents. These database systems should address issues such as assent and consent, should provide information on variation in laws and guidelines across jurisdictions, should include the capacity for interactive communication on numerous situations potentially facing investigators, and should serve as sources of referral for additional assistance.

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3. ***Develop Improved Methods of Neuroimaging to Assess Structural and Functional Status of the Brains of Children and Adolescents Exposed to Drugs.*** Document the feasibility and accuracy of appropriate and acceptable methods for assessing brain structure and function of children and adolescents, with special attention to any or all of the following groups: those exposed to drugs during pregnancy, those passively exposed

during infancy and childhood, and those actively using illicit substances. Documentation should include attention to such matters as technological difficulties and risks, and standardization issues relevant to testing conditions and image analysis.

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4. ***Develop and Refine Methodologies for Drug Use Measurement Among Adolescents.*** Research to develop and refine methodologies for drug use detection and quantification, with special application to the adolescent with HIV infection or at high-risk for HIV infection. This research should address issues of acceptability, reliability, and validity of one or more methods (e.g., interviews, computerized questionnaires, and biological indicators such as saliva or sweat).

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**Other Research Topics Within the Mission of the Institute**

NIDA encourages applications in other areas of research that may not be listed.

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For administrative and business management questions, contact:

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## **NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)**

The NIDCD supports research on the normal mechanisms of, as well as on diseases and disorders of hearing, balance, smell, taste, voice, speech and language. The Institute also supports research related to disease prevention and health promotion. The NIDCD addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders. The NIDCD also supports efforts to create and refine devices that substitute for lost and impaired sensory and communication functions. For more specific information about areas of interest to the NIDCD, please visit our home page at <http://www.nidcd.nih.gov/>.

### **Hearing Program**

Research and development related to hearing aids, cochlear implants, and other assistive devices (e.g., systems designed to improve access to and to increase utilization of computer and other information technologies, telecommunication devices, alerting systems) for individuals with hearing impairments; development of tests and instruments (including DNA-based assays) for the screening and diagnosis of hearing impairment, especially in neonates and infants; development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new outcome measures for assessing the efficacy of treatments of hearing disorders; development of new research tools to aid in the study of the auditory system (e.g., imaging techniques, neuroanatomic tracers, electrophysiologic technology, new animal models); development of viral and non-viral vectors to enable gene transfer to the inner ear; and development of cell type specific probes to examine cell lineage in inner ear regeneration.

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### **Balance/Vestibular Program**

Research to develop and refine tests of balance and vestibular function. Balance disorders affect a large proportion of the population, particularly

the elderly. The vestibular system, with its receptor organs located in the inner ear, plays an important role in the maintenance of one's orientation in space, the control of balance while the body is immobile and in motion, and visual fixation of objects during head movement. Emphasis is on research and development of treatments for balance disorders; development of neuroimaging techniques and biochemical markers of disease in the vestibular system; development of systems to assess balance/vestibular function and for assessing the efficacy of physical rehabilitative regimens for balance disorders; development of drug delivery systems targeting peptidergic molecules in the peripheral vestibular apparatus and the central vestibular circuits for the pharmacologic management of balance disorders; development of a comprehensive software system to assess eye movements associated with the vestibulo-ocular reflex; development of instrumentation and a clinical test protocol for assessing the vestibulo-ocular reflex during locomotion; development of instruments and tests for assessing otolithic function; development of instruments and tests measuring head stability during natural stimulation of the vestibular system; development of perceptual reporting techniques and psychological indices for the clinical assessment of the balance-disordered patient; development of new outcome measures for assessing the efficacy of physical rehabilitative regimens for balance disorders; and development of assistive devices for balance disorders.

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### **Voice, Speech, and Language Programs**

Research on studies of voice and speech disorders focus on determining the nature, causes, treatment and prevention of disorders such as stuttering, spasmodic dysphonia, and dysarthria. Emphasis is on research and development of diagnostic measures and intervention strategies for voice, speech, swallowing, and language disorders; development of communication and other assistive devices for individuals with voice, speech, swallowing, and language disorders; identification and development of computer and animal models for research in communication

disorders; development of new systems for visual communication by individuals who are deaf or severely hearing impaired; development of new systems of communication for individuals with motor impairment; design and development of diagnostic measures or materials for early identification of speech and language impairment in children; development of tests for the assessment of childhood and adult language impairment in multi-cultural populations; development of assessment measures of sign language abilities; development of improved artificial larynges and tracheoesophageal shunts; development of artificial intelligence computer models that simulate normal and disordered speech and language.

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### **Smell and Taste Program**

Research on the study the chemical senses of smell and taste to enhance understanding of how individuals communicate with their environment. Improved understanding of the interaction between chemoreception and food consumption will lead to improved nutrition from birth to old age. Both the olfactory and gustatory systems offer special approaches for understanding fundamental mechanisms of plasticity. Advances in molecular and cellular biology, biophysics, and biochemistry of the olfactory and gustatory systems are paving the way for improved diagnosis, prevention, and treatment of chemosensory disorders. Emphasis is on research and development of diagnostic tools for testing human smell and taste function; intervention strategies for smell and taste disorders; biosensors, electronic noses, and other assistive devices for chemosensory impairments; innovative approaches for obtaining functional expression of mammalian odorant receptors in heterologous cells and for assessing ligand-receptor specificities; development of a chemicals resource for providing chemicals at high purity for chemosensory research; development of a non-invasive drug delivery system using the primary olfactory nerve to target drugs to the central nervous system; development of model systems using stem cell populations from the olfactory and taste sensory organs for the study of neurogenesis; development of readily

administered chemosensory tests for population studies; and development of tests to differentiate trigeminal from olfactory and gustatory stimulation.

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### **Other Research Topic(s) Within Mission of Institute**

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For administrative and business management questions, contact:

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### **NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)**

The NIDCR conducts and fosters research on the etiology, pathogenesis, prevention, diagnosis, and treatment of oral, craniofacial and dental diseases and conditions. For more specific information about areas of interest to the NIDCR, please visit our home page at <http://www.nidcr.nih.gov>.

### **Inherited Diseases and Disorders**

Emphasis is on etiology, prevention, and treatment of craniofacial anomalies such as cleft lip and palate, hemifacial microsomia, malocclusion, and syndromic and non-syndromic disorders that manifest craniofacial defects. This includes inherited and sporadic birth defects as well as acquired disfigurement and their effects on functions of the craniofacial region.

- A. Develop and operate registries to track craniofacial birth defects, diagnosis techniques, treatment protocols, and outcome assessments.
- B. Develop and operate tissue banks and/or DNA libraries of samples from patients with craniofacial birth defects and from unaffected relatives to aid in prospective and retrospective epidemiology and linkage studies to facilitate the discovery of genes involved in craniofacial dysmorphologies.
- C. Production of genetic and immunological markers specific for developing craniofacial tissues (e.g., stage specific markers for discrete populations of premigratory, migratory, and differentiating neural crest cells).
- D. Develop early pregnancy genetic tests to screen fetal cells in maternal blood for genetic mutations involved in inherited syndrome and non-syndrome craniofacial defects.
- E. Develop more efficient methods, materials, and appliances for orthodontic tooth movement.
- F. Develop instrumentation to improve the diagnosis and treatment of inherited and acquired craniofacial defects.
- G. Develop instrumentation and methods to more accurately measure craniofacial growth in order to assess normal growth patterns as well as the effects of treatment procedures.
- H. Develop animal models possessing specific genetic craniofacial anomalies for use in studies on the etiology of disease, gene regulation, gene/environment analysis, and gene-product function and development of treatment protocols.
- I. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

### **Infectious Diseases**

Research relating to the etiology, pathogenesis, prevention, diagnosis and treatment of infectious diseases of the oral cavity is supported by the NIDCR. This includes research on practical ways to effectively use the host immune system to prevent or treat oral infectious diseases and microbial-induced inflammation. Infectious diseases of the oral cavity include caries,

periodontitis, candidiasis, peri-implantitis, pulpitis, and various viral and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations of HIV infection and AIDS.

- A. Develop improved instrumentation, methodology, biomarkers or molecular probes for the rapid diagnosis and measurement of infectious diseases.
- B. Develop diagnostic tests to determine host susceptibility to oral infections.
- C. Develop ways to overcome or eliminate the risk of oral infections in persons who smoke or chew tobacco, drink alcohol, are immunosuppressed, have diabetes, are malnourished or are psychologically stressed.
- D. Explore novel methods or agents to eradicate oral biofilms (dental plaque) on teeth, oral soft tissues, and dental implants without adversely affecting the normal oral flora.
- E. Isolate, synthesize or prepare new antibiotics and antimicrobial agents that can overcome bacterial and fungal resistance to current compounds. Formulate combinatorial drug regimens to attack microbes growing in oral biofilms (dental plaque).
- F. Develop controlled release drug delivery systems for the prevention and control of oral infectious diseases.
- G. Develop biological response modifiers or other immunological approaches to reduce or eliminate microbial-induced chronic inflammation or the tissue destruction associated with chronic inflammation.
- H. Provide inexpensive services and resources to sequence and exploit the genome of oral bacterial pathogens.
- I. Develop improved animal or in vitro models of oral infectious diseases to enable evaluation of pathogenesis and therapies.
- J. Develop ways to interfere with microbial colonization and growth through the use of antimicrobial agents, chemotherapy or vaccines.
- K. Establish needed services that will benefit oral health care providers or research laboratories involved in the study or treatment of oral infectious diseases. Such

services might be facilities for: software design; design and preparation of peptides and molecular probes; establishing and growing hybridomas; testing, breeding or caring for research animals; determining antimicrobial sensitivity of microbes growing in biofilms (dental plaque) to drugs and antibiotics; or high technology imaging.

- L. Establish practical methods to increase host immune and non-immune defenses against infectious diseases (e.g., vaccines, biological response modifiers). Develop adjuvants to stimulate mucosal immunity. Identify and characterize target antigens for vaccines.
- M. Develop technologies for detecting and eradicating microbial biofilms in dental equipment.
- N. Develop methods for early diagnosis of oral opportunistic infections in asymptomatic individuals exposed to HIV.
- O. Develop diagnostic tests utilizing whole saliva and oral biopsies for examination of local immune responses and for the and assessment of disease progression
- P. Develop computer programs to model biologically active peptide regions of oral components that have anti-fungal, anti-bacterial and anti-viral activities.
- Q. Develop substitutes of naturally occurring chemicals (phytochemicals) known to have a role in controlling opportunistic infections induced by HIV.
- R. Develop synthetic peptides and recombinant proteins of oral components with anti-fungal, anti-bacterial and anti-viral, specifically HIV, activities.
- S. Develop controlled release delivery systems for local delivery of synthetic peptides recombinant proteins with anti-fungal, anti-bacterial and anti-HIV activities and of drugs.
- T. Develop and/or improve innovative and highly sensitive molecular techniques to examine changes of cytokines and other immune regulators, and of viral load in oral tissues and fluids.

### **Neoplastic Diseases**

Emphasis is on the prevention, etiology, initiation, early detection, progression and

treatment of pre-malignant and malignant oral lesions as well as the invasion and metastasis of oral cancer cells.

- A. Develop immunological methods, imaging techniques or genetic markers for the early detection, diagnosis and prognosis of pre-malignant oral lesions and oral carcinomas.
- B. Develop methods for the rapid and specific detection of viruses implicated in the etiology of oral cancer as well as the detection of viral genes in pre-malignant and malignant oral lesions.
- C. Develop vaccines effective against viruses suspected to be etiologic agents in the induction of pre-malignant and malignant oral lesions.
- D. Develop new techniques for the evaluation of chromosomal changes in oral cancer.
- E. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant oral lesions.
- F. Develop technology for the genetic therapy of oral carcinomas.
- G. Develop animal models of localized and metastatic oral squamous cell carcinomas.
- H. Develop methodologies for prevention of the metastasis of oral cancer cells.
- I. Identify and isolate novel oncogenes and tumor suppressor genes.
- J. Develop regimens for the alleviation of the oral complications of cancer therapy.

### **Chronic Disabling Diseases**

Emphasis on research on chronic disabling diseases, including injury, of the oral-cranio facial-dental areas including neuropathies and neurodegenerative disorders, osteoporosis and other diseases of bone and connective tissue, diseases of the temporomandibular joint, autoimmune diseases (e.g., Sjogren's syndrome) which influence and which are influenced by diseases of the oral cavity, and reciprocal influences of other systemic diseases such as diabetes and cardiovascular diseases and the oral cavity.

- A. Develop improved measures for measuring chemosensory, tactile, kinesthetic, or proprioceptive function involving craniofacial structures. Such measures

may be useful in screening for deficits, improving diagnosis, or for evaluating response to dental treatments or interventions.

- B. Develop improved measures for assessing oral-motor coordination or oral behaviors (e.g., swallowing, masticatory efficiency). Such measures will facilitate screening for deficits in special populations, improving diagnosis, or evaluating response to dental treatments or interventions.
- C. Develop improved biomarkers or treatments for neuropathic conditions or neurodegenerative conditions affecting oral-craniofacial tissues or structures.
- D. Develop assays facilitating reliable evaluations of relationships between hormonal or chronobiological variations and other risk factors, as these relate to onset or exacerbation of pain symptoms.
- E. Develop improved in vitro or animal models for evaluating biomechanical, wear, functional or systemic responses associated with TMJ devices or engineered tissues.
- F. Develop improved in vitro or animal models for assessing pathobiological changes in the TMJ or masticatory muscles; improved biochemical markers of joint degradation. Such studies could have eventual relevance to improving diagnosis or treatment in humans.
- G. Develop innovative approaches to reduce foreign body reactions or to improve surgical outcomes for prosthetic devices or bone grafts received subsequent to failed alloplastic TMJ implants
- H. Develop safe and effective biomaterials or procedures useful in repairing the temporomandibular joint (TMJ) following trauma, degenerative or inflammatory diseases processes, or iatrogenically-induced pathology (e.g., failed TMJ implants).
- I. Develop diagnostic reagents and tests necessary to effectively use changes in saliva to diagnose and monitor specific disease processes, drug therapy, genetic defects, nutritional status, and age-specific therapy.
- J. Develop and characterize immortalized normal human and rodent salivary gland

epithelial cell lines with appropriate phenotypic expression.

- K. Develop artificial saliva and/or drugs (sialogogues) for the treatment of xerostomia and develop controlled release delivery systems for their delivery at desired sites.
- L. Develop non-invasive methods for the determination of the efficacy and safety of artificial saliva, sialogogues and of their delivery vehicles.
- M. Develop viral and non-viral vectors for salivary gene therapy and gene therapeutics.
- N. Develop recombinant proteins and synthetic-peptides of salivary molecules with known activities as well as vehicles for their delivery.
- O. Evaluate the adverse effects of oral microbes on systemic diseases and conditions (e.g., diabetes, cardiovascular diseases), and develop intervention strategies to alleviate these effects.
- P. Develop apparatus for craniofacial bone distraction that is contained entirely within the oral cavity.
- Q. Develop more efficient methods, materials, and devices for prevention of injuries to the teeth, mouth, and face during athletic activities.
- R. Develop more efficient methods, materials, and appliances for orthodontic tooth movement.
- S. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

### **Biomaterials, Biomimetics, and Tissue Engineering**

Emphasis is on the development of natural and synthetic materials to be used for the repair, regeneration, restoration and reconstruction of oral tissues and organs; on the development and improvement of evaluation and measurement systems for the characterization of implanted material properties; on their interactions as well as on their performance under the severity of the biological environment; and finally on the development and/or improvement of new alloy combinations, especially those that are mercury free.

- A. Develop strategies for site-specific focus of repair and regeneration dynamics (e.g., smart implants to specifically attach the appropriate reparative cells).
- B. Establish libraries of structural recognition epitopes (peptides, carbohydrates) to screen biological activities (e.g., bacterial adherence to soft and hard oral tissues).
- C. Develop non-destructive methods for the characterization of material properties in vivo and in vitro.
- D. Develop synthetic analogues of oral/craniofacial tissues and organs.
- E. Develop more sensitive methods to determine and measure the interactions of materials with biological systems (e.g., material biocompatibility and bioactivity in the oral environment).
- F. Optimize imaging techniques for describing the architecture of oral tissues and structures.
- G. Develop computer and mathematical modeling systems capable of mimicking biological tissues and of evaluating material designs.
- H. Develop novel techniques for ensuring sterility of biomimetic structures prior to implantation.
- I. Develop delivery systems that are compatible with host immunity; consider hybrids and artificial vectors as well as viral and non-viral gene delivery systems with cell-type selectivity.
- J. Develop in vitro methods that predict immunogenicity to vectors used for gene transfer as well as for biomaterials.
- K. Develop improved materials, designs (nanotechnology principles) and surgical techniques for artificial implants to support replacement of dental, oral and craniofacial tissues and organs.
- L. Develop new and improved instruments and techniques for the diagnosis and treatment of TMDs.
- M. Develop improved composite materials and adhesive sealants suitable for restoring crowns of posterior teeth and exposed roots of teeth.
- N. Develop new non-mercury containing filling materials.

## **Behavior, Health Promotion and Environment**

Research on patterns and outcomes of acute and chronic oral diseases, and on oral and systemic disease co-morbidities within the population; socio-environmental or behavioral factors which influence host response, individual behaviors, care providers' behaviors, clinical decision making, information transfer technologies, dental utilization, health care delivery, treatment or health care outcomes and research which integrates biological or molecular determinants of health with sociobehavioral determinants.

- A. Develop improved systems, which accelerate effective transfer of scientific information to health professions.
- B. Develop new computer-based or other technologies to improve the quality of clinical decision-making or encourage increased congruence between current knowledge and actual clinical practices.
- C. Develop reliable, sensitive, cost-effective measures for assessing oral health status in populations or population subgroups.
- D. Develop and standardize improved outcome measures for use in assessing short or long-term impacts of oral treatments or health promotion interventions.
- E. Develop convenient, reliable, sensitive, cost-effective biomarkers for diurnal variations, other chronobiological variations, or cyclic variations in hormonal levels utilizing information drawn from oral tissues.
- F. Develop and evaluate the reliability and impacts of devices or biomarkers assessing patient compliance with preventive or therapeutic regimens or measuring subject compliance within clinical trials.
- G. Develop and evaluate innovations in headgear or other protective equipment to reduce dentofacial injuries.

## **Other Research Topic(s) Within Mission of Institute**

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## **NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)**

The NIDDK supports research in diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic and hematologic diseases. For additional information about areas of interest to the NIDDK, please visit our home page at <http://www.niddk.nih.gov>.

### **Diabetes, Endocrinology and Metabolic Diseases**

The Division of Diabetes, Endocrinology and Metabolic Diseases supports basic and clinical research on the etiology, pathogenesis, prevention, diagnosis, and treatment of diabetes mellitus and its complications; endocrine diseases; osteoporosis; cystic fibrosis, and other metabolic disorders; as well as research on basic endocrine and metabolic processes. Research topics of potential interest to small businesses include, but are not limited to:

- A. Development and characterization of animal models for diabetes, obesity, or complications of diabetes.
- B. Development of non-invasive or minimally invasive methods for monitoring blood glucose; implantable glucose sensors; improved insulin delivery methods or devices; improved insulin formulations; or integration of sensor and delivery systems to create an artificial pancreas.
- C. Development a cell culture model of the human pancreatic beta cell that will have the following salient features: (1) stably maintain its physiologic responsiveness to glucose and othe secretagogues, (2) accurately reflect in vivo signaling through cell surface and nuclear receptors relevant to the regulation of insulin production and secretion, (3) maintain responsiveness to growth factors and cytokines normally active in the development and maintenance of the pancreatic beta cell, and (4) retain contact growth inhibition as in the in vivo situation.
- D. Development of novel methods for beta-cell expansion, use of islet stem cells for allografting, or short or long term culture of pancreatic tissues for islet cell transplantation.
- E. Development of antibodies to cell surface markers on mammalian stem/progenitor cells from the pancreas that will facilitate the prospective identification and purification of these cells.
- F. Development of quantitative clonogenic assays both in vivo and in vitro that will allow characterization of potential stem/progenitor cells of the pancreas.
- G. Development of tests for islet viability, using functional genomics, proteomics, or other methods, and of improved methods to enhance viability of islets prior to implantation, methods to improve engraftment of islets, or methods to protect isle grafts though immunomodulation/tolerance induction or immuno-isolation.
- H. Development of improved methods for whole pancreas transplantation such as improved protective measures, less toxic drugs, immunomodulation or tolerance induction.

- I. Development of novel or improved methods for monitoring metabolic control in diabetes.
- J. Development of non-invasive imaging methods for in vivo measurement of pancreatic beta cell mass, function, inflammation or perfusion, for use in both endogenous pancreas and transplanted pancreatic tissue/islet cells.
- K. Development of assays to detect viruses in pancreatic or lymphoid tissue to study the etiology of type 1 diabetes.
- L. Development of techniques or products useful in prevention of type 1 diabetes, including strategies for vaccination or immunomodulation/tolerance induction.
- M. Development of novel methods for the large scale production of GAD or other potential immunoprotective proteins for use in clinical trials.
- N. Development of improved methods of HLA typing, assays for predictive autoantibodies, and other tests for use in identifying patients at risk of developing type 1 diabetes.
- O. Development and testing of new strategies to detect the onset and monitor the progression of the late complications of diabetes, particularly neuropathy.
- P. Development of surrogate markers for identification of disease states and disease progression, and for use as endpoints in clinical trials of diabetes and its complications; osteoporosis; and cystic fibrosis.
- Q. Development and testing of new strategies to prevent the late complications of diabetes, including new modalities to prevent the development of or promote complete, rapid healing of diabetic foot ulcers.
- R. Development of DNA chip array technologies and other new methods to identify and analyze differential gene expression in cells and tissues affected by diabetes mellitus and its complications.
- S. Development of new vectors, gene inactivation techniques, and other novel methodologies for gene therapy of diabetes and its complications.
- T. Development of methods to maximize the ability of patients and providers to implement recommended therapy for diabetes and achieve desirable outcomes, including strategies to enhance diabetes self-management, to address social and cultural barriers to adherence, to improve communication between patients and care providers, and to develop alternative models of health care delivery (such as computer-aided management or telemedicine).
- U. Development of new drugs or innovative strategies to reduce peripheral insulin resistance in type 2 diabetes.
- V. Development of quantitative measures for the evaluation of health behavior modification programs, such as methods to measure dietary intake and physical activity, in the prevention and control of diabetes.
- W. Development of non-peptide agonists and antagonists for hormone and neuropeptide receptors with potential utility in structural studies or for therapeutic use in the treatment of endocrine disorders, including obesity.
- X. Identification of new ligands for previously unclassified (orphan) receptors and/or partial agonists or antagonists with therapeutic potential.
- Y. Development of Selective Receptor Modulators (SRMs) with tissue-specific action.
- Z. Development of nonradioactive techniques for measuring hormones.
- AA. Development of new techniques for simultaneous measurement of multiple hormones in a single solution.
- BB. Development of new tests or reagents for diagnosis of endocrine disorders.
- CC. Development of new or improved technologies for physiologic and metabolic measurements in transgenic mice, including miniaturized assays, metabolic cages, and new imaging strategies.
- DD. Development of analytical and display tools which could be used with large clinical data sets, imaging data, microarray assays, or genomic data.
- EE. Development of new, automated techniques for protein crystallization.

FF. Development of new approaches to the modeling, analysis, and prediction of three-dimensional protein structure (including membrane proteins).

GG. Development of novel methods for determination of the three-dimensional structure of transporter proteins or protein families.

HH. For cystic fibrosis, NIDDK is interested in research in the following areas:

1. Development of specific inhibitors of CFTR.
2. Development of measures or endpoints that can be used for evaluating the success of therapy for cystic fibrosis, including gene therapy.
3. Development or improvement in diagnostic tests for cystic fibrosis.
4. Animal or cell models useful for the study of cystic fibrosis, including use of transgenic technology.
5. Identification or characterization of potential therapeutic modalities capable of ameliorating the molecular defects in cystic fibrosis, including agents to improve trafficking and function of mutant CFTR, to enhance function of channels which may serve as alternatives to CFTR, to enhance other cell processes impaired by mutations in CFTR, and to correct the molecular defects (such as impaired anti-microbial peptide activity) leading to the infection and inflammation characteristic of cystic fibrosis.
6. Development or improvement in approaches to gene therapy for cystic fibrosis through optimization of gene delivery systems to improve tropism for target cells, increase the efficiency and duration of transgene expression, and mitigate potential toxicity, or evaluation of safety and efficacy of methods for gene therapy of cystic fibrosis in animals models or human subjects.
7. Development of products useful in assessing or improving nutritional status in patients with cystic fibrosis, including improvement of pancreatic enzyme preparations.
8. Development and validation of effective strategies to improve compliance with

therapy and promote health-enhancing behavior for people with cystic fibrosis.

9. Development, testing, and validation of educational materials for use in conjunction with (1) carrier detection or (2) neonatal screening or other methods for diagnosis of cystic fibrosis useful for helping people understand the risks, benefits and imitations of the test and the interpretation of the results.

II. For other inherited metabolic disorders, e.g., defects of urea cycle enzymes and enzymes of purine and pyrimidine metabolism, glycogen and lipid storage diseases, organic and aminoacidurias, NIDDK is interested in research leading to:

1. Development of restriction fragment length polymorphisms and polymerase chain reaction techniques for diagnostic reagents and tests and adaptation of these techniques to prenatal diagnosis in fetal cells isolated from maternal blood.
2. Production of large quantities of enzymes by recombinant DNA technology in bacteria cell lines or transgenic animals as a first step toward production of an orphan drug.
3. Design and synthesis of chemical "activators" for mutant enzymes.
4. Design and synthesis of new, stabilized, biological active peptides and proteins useful for enzyme replacement therapy.
5. Development of stabilized enzymes through in vitro site-directed mutagenesis or enzymatic modification.
6. Development of animal models of genetic diseases that mimic the pathophysiology of the human disease and can be used to assess treatments.
7. Improvements in transfection efficiency, level of gene expression or duration of gene expression for currently used gene therapy vectors.
8. Development of packaging cell lines which will package replication defective viruses to higher titers or package viral DNA with new or altered viral envelope proteins to improve cell targeting.

9. Development of new vectors including AAV, lentivirus or Herpes virus with improved ability to transduce non-dividing cells such as hematopoietic stem cells, neurons, hepatocytes or lung epithelium.
10. Development of efficient homologous recombination techniques to allow insertion of a corrected gene in its normal location.
11. Improvements in experimental delivery systems such as liposomes or conjugates for receptor-mediated endocytosis to increase efficiency of targeted DNA delivery and increase duration of expression.

### **Digestive Diseases and Nutrition**

The Division of Digestive Diseases and Nutrition supports research on the function, diseases and disorders of the digestive tract; the esophagus, stomach, intestine, colon, anorectum, pancreas, liver, gallbladder, and biliary tract; basic, clinical and behavioral research on nutrition and obesity as well as information transfer in the field of digestive diseases and prevention of obesity. Innovative investigator-initiated projects that are not mentioned below are encouraged. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of a better method for measuring food intake patterns of individuals that could replace recall.
- B. Development of better methods for assessing overall nutritional status.
- C. Development of a non-invasive breath or blood test to accurately measure dietary fat intake.
- D. Development of biological measures, such as serum or urine tests, for long-term dietary consumption of specific nutrients.
- E. Development of safe drugs or herbal products that inhibit appetite.
- F. Development of better means of assessing energy intake and/or energy expenditure (i.e., physical activity), e.g., a device to estimate movement and relate this to calories expended with the goal of impacting behavior and preventing obesity.
- G. Development of computerized interventions for weight-loss/maintenance and/or increasing physical activity such as hand-held computers and web-based programs.
- H. Development of devices/equipment/interventions to encourage "activity" while performing sedentary work.
- I. New technologies for quantitative assessment of intra-abdominal fat; emphasis on technologies that are non-invasive, minimize the use of ionizing radiation, and have the capability of being adapted for use in the usual health care settings.
- J. Development of more economical methods to produce 18-labelled oxygen for use in energy expenditure studies and/or body composition studies using doubly labeled water.
- K. Development of better means to detect food borne pathogens with the goals of (1) preventing their inclusion in foodstuffs and (2) better treatment of acute infections.
- L. Development of new genetic screening methods for detection of inherited digestive and nutritional disorders, e.g., hemochromatosis, Wilson's disease, Crigler-Najar syndrome, Alagille syndrome.
- M. Development of a non-invasive means of localizing GI bleeding beyond the duodenum that is more sensitive than the Tc-RBC test.
- N. Development of methods for gastrointestinal endoscopy without the need for sedation.
- O. Development of molecular probes for the diagnosis of mucosal dysplasia in inflammatory bowel disease.
- P. Development of new techniques, including non-invasive imaging, to measure motility/intestinal transit at various sites within the gastrointestinal tract.
- Q. Development, using rationale drug design techniques, of agents that interact with L-type calcium channels or with delayed rectifying potassium channels to treat motility disorders (pseudo-obstructive disorder, chronic constipation, and slow bowel transit).
- R. Development and validation of herbal, ayurvedic, Chinese traditional, Kampo or other treatments for common GI ailments

- and liver diseases such as motility disorders, IBD, and cirrhosis.
- S. Development of pharmaceuticals from herbal preparations of promise for therapy of digestive diseases, including liver diseases, involving isolation of active components, preparation of pharmacologically pure preparations, and testing for pharmacokinetics and activity in humans.
  - T. Development of novel antifibrotic therapies for progressive liver failure.
  - U. Development of agents that would protect the gut epithelium from the damage caused by chemotherapeutic agents.
  - V. Development of agents to promote the repair of gut epithelium barrier function, e.g., as needed following chemotherapy.
  - W. Development of techniques for the preservation and transplantation of small intestine and pancreas.
  - X. Development of non-invasive measures of pancreatic exocrine function.
  - Y. Development of drugs for dissolving gallstones in vivo.
  - Z. Development of a test for determining the hepatotoxic potential of drugs, agents or additives that is more sensitive than testing in mice and reflects the human response to the test compound.
  - AA. Development of animal models to study hepatotoxic agents.
  - BB. Improvements to existing imaging systems, or development of new ones, to allow non-invasive detection of fibrotic, necrotic, inflamed, and fatty livers prior to transplantation.
  - CC. Development of non-invasive techniques to detect liver disease.
  - DD. Development of non-invasive devices/techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.
  - EE. Development of a rapid, non-invasive diagnostic test for biliary atresia.
  - FF. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

- GG. Development of non-occluding stents for use in the biliary tract and in transjugular intra-hepatic porto-systemic shunts (TIPS).
- HH. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.
- II. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.
- JJ. Development of molecular standards for Hepatitis C virus quantitation and typing.
- KK. Development of molecular standards for Hepatitis B virus quantitation and typing.

### **Kidney, Urologic and Hematologic Diseases**

The Division of Kidney, Urologic, and Hematologic Diseases supports research into basic mechanisms of organ and tissue function and into the diseases of the kidney, urologic and hematologic systems. Projects to help develop an understanding of the physiology, pathophysiology, and related diseases of the kidney, urinary tract, and blood and blood forming systems so that rational treatments and means of prevention and/or arrest of diseases may be devised. Support for advances in the technology of cell and molecular biology that will enhance research in kidney, urologic and hematologic diseases is encouraged. Research opportunities of interest to small businesses include, but are not limited to:

- A. Development of a genomic toolbox for study of kidney, prostate, bladder, or red cells which would include:
  1. Library generation and gene identification from whole organ or rare compartments in normal, developing, or injured tissues;
  2. Strategies to deal with the anatomical complexity, increase the representation of low abundance transcripts, or decrease the redundant sequencing of over-represented or known genes;
  3. Bioinformatic tools;
  4. Flexible databases useful for designing organ-specific databases and web sites;
  5. Techniques for visualizing RNA distribution within cells or tissues; and

6. New methods to acquire material from archival samples.

#### KIDNEY

- A. Development of monoclonal antibodies specific for the individual cell types of the renal glomerulus, proximal and distal tubules, loops of Henle, and collecting ducts.
- B. Development of both data and cell banks of diabetic kidney disease families for use by the research community.
- C. Studies aimed at discovering a genetic mechanism of patients known to have IgA nephropathy.
- D. Studies researching Atrial Natriuretic Factor (ANF) as a potential pharmacological tool to intervene in disorders of renal hemodynamics, blood pressure, and extracellular volume regulation.
- E. Means to achieve a more stable physiologic homeostasis in maintenance dialysis therapy to overcome the physiologic consequences of intermittent hemodialysis through the:
  1. Improvement of blood access to permit continuous access to the circulation; or
  2. Development of means to provide for continuous anticoagulation.
- F. Studies to improve the efficiency of maintenance dialysis:
  1. Development of innovative methods to produce more efficient and less morbid forms of renal dialysis (e.g., GI dialysis, artificial kidney).
  2. Studies on biocompatibility of artificial kidney membranes, in surface sensitive proteins, complement, and clotting mechanisms.
  3. Development of new agents for sterilizing dialysis membranes.
  4. Development of new dialysis membranes to diminish the duration of dialysis treatments.
- G. Improved techniques of preservation and storage of kidneys intended for transplantation.
- H. Development of material(s) for construction of urinary catheters that may reduce the incidence of infection in the urinary tract.
- I. Studies to determine which agents might contribute to the progression of abnormal cell growth in polycystic kidney disease, including growth hormones and dietary elements.
- J. Development of improved renal imaging techniques, differential renal function assessments and diagnostic distinction between benign and malignant parenchymal diseases.
- K. Development of new therapies for rare diseases of the kidney and urinary tract.
- L. Studies researching causes of interstitial cystitis.
- M. Computer-Assisted Diagnosis and Teaching in Acid-Base and Electrolyte Disorders.
- N. Development of methods to provide early diagnostic tools, preventative measures, and treatment modalities for Acute Renal Failure.
- O. Development of new non-invasive methods for measuring kidney function:
  1. Reliable, non-invasive, non-radioactive methods of measuring glomerular filtration rate (GFR);
  2. Identification and description of physiologic compounds that are filtered by the kidney, but neither secreted or reabsorbed;
  3. Identification of serum factors released by damaged kidney cells;
  4. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity;
  5. Development of new markers of early kidney dysfunction.
- P. Relationship between microalbuminuria and GFR including change in evaluate rate of growth.
- Q. Population studies of kidney and urologic disease:
  1. Distribution of various types of kidney and urologic disease in the United States;
  2. Risk factors for developing kidney dysfunction, hypertension and kidney disease;

3. Ethnic variation in distribution, and risk factors for kidney and urologic diseases;
  4. Markers predictive of development of end-stage kidney disease.
- R. Development of sensitive techniques to identify open reading frames of chromosomes in specialized tissues, such as the prostate or renal glomerulus; e.g., methods for developing a cDNA library with mRNA as a starting material.

#### UROLOGY

- A. Study of the effect of growth factors, hormonal concentrations and other biochemical stimuli on the growth of prostatic tissue. Analyses of factors responsible for initiation and progression of Benign Prostatic Hyperplasia (BPH).
- B. Development of animal or in-vitro models for the study of stromal - epithelial interactions in BPH.
- C. Assessment of factors responsible for Benign Prostatic Hyperplasia (BPH) induced uropathy.
- D. Host-parasite and bacteria-urothelial cell interactions involved in urinary tract infection.
- E. Kinetics of renal stone formation, such as characterization of growth and dissolution, or crystal growth inhibition, and definition of reliable biochemical profiles of stone forming patients.
- F. Development of additional therapeutic agents for prevention and/or treatment of urolithiasis.
- G. Neuropharmacological-neurophysiological assessments in urodynamics.
- H. Development of culture conditions for in vitro culture of cells from benign prostatic hyperplasia.
- I. Development of serum or urine markers that correlate with prostate size to evaluate rate of growth.
- J. Development of non-invasive instrumentation which can detect early onset of bladder instability associated with diabetes mellitus.

#### HEMATOLOGY

- A. Identifying biochemical, immunological, morphological, and genetic criteria for stem cells and progenitor cells.
- B. Improving the methodology for hematopoietic stem cell purification.
- C. Isolation, purification, and characterization of cellular receptors for hematopoietic growth factors.
- D. Development of in vitro and animal models for study of bone marrow depression associated with retroviral infection.
- E. Safe retroviral agents for gene insertion studies in hematopoietic systems.
- F. Developing protocols for routine isolation of highly purified stem and progenitor populations.
- G. Identifying new methods to assay stem and progenitor cells with short- and long- term repopulation models amenable to serial examination.
- H. Identifying and defining the cytokines and growth factors that have a positive or negative influence on the behavior of hematopoietic stem cells.
- I. Determining the role of cell-cell interactions between stromal and stem cells in determining the capacity of the latter for self-renewal and differentiation.
- J. Identifying and cloning the homing receptors on hematopoietic stem and progenitor cells.
- K. Defining the factors or growth conditions that modulate self-renewal, differentiation, or apoptosis of stem cells using purified cells, recombinant growth factors and serum-free conditions.
- L. Developing assays for quantitation of retroviral receptor molecules on stem cells and determining conditions for influencing their level of expression.
- M. Developing new methods for stable insertion of genes into purified stem cell populations.
- N. Elucidation of factors such as DNA elements, DNA binding proteins, nuclear matrix, signal transduction mechanisms, stromal or cell-surface protein interactions that may contribute to lineage-specific

differentiation by modulation of gene expression.

- O. Development of animal models for hematologic diseases.
- P. Identification and/or characterization of factors controlling gene expression in differentiation.
- Q. Identification and/or characterization of factors controlling the hematopoietic cell cycle.

#### **Other Research Topic(s) Within Mission of Institute**

For additional information on research topics, contact:

##### *Diabetes, Endocrinology and Metabolic Diseases*

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##### *Digestive Diseases and Nutrition*

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#### **NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)**

Human health and human disease result from three interactive elements: environmental factors, genetic susceptibility and age. The mission of the NIEHS is to reduce the burden of human illness and dysfunction from environmental causes by further understanding each of these components and how they interrelate. NIEHS achieves its mission through a multidisciplinary biomedical research program, prevention and intervention efforts, and a communication strategy that encompasses training, education, technology transfer and community outreach. The ultimate goal of the NIEHS activities is to define and understand the mechanism of action of environmental agents on human health and to transfer this knowledge to the public benefit. Thus, as a part of this mission, NIEHS supports research and training focused on the identification, assessment and mechanism of action of agents in the environment that are potentially harmful to human health.

For additional information about areas of interest to NIEHS, visit our home page at <http://www.niehs.nih.gov>.

- A. Development and validation of alternative designs/methods for toxicity testing assessment.
  - 1. Transgenic animals
  - 2. Non mammalian models
  - 3. Invertebrate models
  - 4. Organ/cell/ tissue culture models
  - 5. Computer generated models that will reduce the use of animal testing
  - 6. Animal stem cell models
  - 7. Breeding/selection of sensitive models
  - 8. Models that will reduce animal pain and suffering
  - 9. Molecular fingerprinting using microarrays

These models may be developed for assessing mutagenicity, carcinogenicity, reproductive-, immuno-, developmental-, neuro-, skin-, ocular-, or general toxicity or estrogenicity/androgenicity (i.e., endocrine active compounds).

- B. Development of products/devices for measuring exposure to toxic agents.
1. Personal monitors to detect exposure to toxic agents.
  2. Miniaturization of sampling instruments and pumps for use with children.
  3. Identification of toxic products/metabolites in blood, urine or saliva that could be used for screening large populations for exposure.
  4. Biomarkers of exposure/toxicity or effect.
  5. Immunologic methods such as monoclonal antibodies (ELISAs) for quantitative detection of environmental contamination.
  6. Noninvasive imaging techniques to detect toxicants/metabolites or toxicity.
  7. Nanotechniques to detect and assay environmental agents and their metabolites.
- C. Development and validation of bioengineering technology (including nanotechnology) for use in environmental health sciences.
1. Microarray technology for assessing gene or protein fingerprints of exposure to environmental agents.
  2. Human breath analysis for metabolic phenotyping.
  3. Microarray technology to determine global gene expression and tissue specific gene expression over time.
  4. High throughput fingerprinting of genetic polymorphisms for use in large scale human studies.
  5. Miniaturization of high throughput technology for gene/protein expression for detection of toxicant exposure in field studies.
  6. Real time imaging and monitoring techniques of biological processes and the effects of toxicants.
  7. Hardware/software for the analysis of pathologic data such as an automated method for counting ovarian follicles and assessing their biological state.
- D. Development of animal models that mimic the human disease process (for example:
- long term onset, genetic susceptibility to environmental exposure).
1. Parkinson and other neurodegenerative diseases.
  2. Autoimmune and other immunologic diseases.
  3. Endocrine related diseases.
  4. Cardiovascular/gastrointestinal/liver/kidney diseases.
- E. Development of educational materials related to Environmental Health Sciences
1. Interactive programs or databases for learning about environmental health issues(K-12).
  2. Educational materials on subjects such as risk assessment, pesticides or endocrine disruptors, toxicology, basic cell biology, air/soil/water quality and health impacts (K-12).
- F. Additional products related to the NIEHS mission of protecting/improving the public health by reducing the risk of toxicity due to exposure to environmental agents
- Other Research Topic(s) Within Mission of Institute**
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- D. Development of animal models that mimic the human disease process (for example:

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## **NATIONAL EYE INSTITUTE (NEI)**

The NEI supports research with respect to blinding eye diseases, visual disorders, mechanisms of normal visual function, preservation of sight, and the special health problems and requirements of individuals with impaired vision. The NEI's programs are described in extensive detail in documents which are available from the Institute. Examples of some research topics from the recently published NEI's Plan (Vision Research - A National Plan: 1998-2003) for each program area that may be of interest to small business concerns are listed below.

For additional information about the research programs of the NEI, please visit our home page at <http://www.nei.nih.gov>.

### **Retinal Diseases Program**

Research and development of new therapeutic approaches for ocular inflammatory diseases and to inhibit abnormal proliferation of the retinal and choroidal blood vessels; development of better methods of diagnosing and treating diabetic retinopathy and other vascular diseases of the retina and choroid; development of non-invasive techniques for early diagnosis of macular degeneration and other retinal degenerative diseases; development of instruments and procedures for improved surgical management of retinal detachments.

### **Corneal Diseases Program**

Research and development of new therapeutic agents for the treatment of corneal diseases; development of innovative methods of drug delivery for ocular surface disorders; development of new biomaterials for corneal prostheses; development of instruments and procedures for correcting the refractive power of the cornea and measuring the cornea's optical and physiological properties.

## **Lens and Cataract Program**

Research and development of therapeutic agents for the prevention of cataract; development of new approaches in the post-operative management of cataract surgery; development of new surgical instruments for cataract extraction and biomaterials for replacement of the natural lens.

## **Glaucoma Program**

Research and development of new therapeutic agents, instruments, and procedures for the diagnosis and treatment of glaucoma; development of non-invasive methods to measure changes in the optic nerve head and retinal fiber layer.

## **Strabismus, Amblyopia, and Visual Processing Program**

Research into the identification and characterization of growth factors which facilitate regeneration of visual nerve axons; development of innovative techniques to study factors that facilitate regeneration and guidance of developing or regenerating nerve fibers; development of new approaches using imaging techniques, such as PET and MRI, to localize lesions and test the functioning of specific parts of the visual system, especially those involved in higher order visual processing.

## **Visual Impairment and Its Rehabilitation Program**

Research and development of instruments and methods to better specify, measure, and categorize residual visual function; development and evaluation of optical, electronic, and other devices that meet the rehabilitative needs of persons who are blind or have low vision.

## **Other Research Topic(s) Within Mission of Institute**

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## **NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)**

The NIGMS supports research and research training in the basic medical sciences and related natural and behavioral sciences and in specific clinical areas (i.e., clinical pharmacology, trauma and burn injury, and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components.

For additional information about areas of interest to the NIGMS, please visit our home page at <http://www.nigms.nih.gov>. This site includes staff contact information by program area ([http://www.nigms.nih.gov/nigms\\_staff/contact.html](http://www.nigms.nih.gov/nigms_staff/contact.html)) It also includes links to program announcements that highlight NIGMS areas of special emphasis (<http://www.nigms.nih.gov/funding/funding.html>).

In some cases, these announcements specifically mention the SBIR and STTR grant mechanisms, in most cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in these announcements.

### **Division of Cell Biology and Biophysics**

Research on membrane synthesis, structure, and function; membrane models; membrane transport; cell division; cell organization; cell motility; and biophysics of proteins, nucleic acids, and biological assemblies, as well as the development of instrumentation, components, and methods for the analysis of cellular components and macromolecules by imaging, spectroscopy, and diffraction analysis.

SBIR and STTR proposals on the application of cell biology, biophysics, biochemistry, physics, mathematics, engineering, and chemistry to biomedical problems, and the development of instrumentation to facilitate research in cell biology and biophysics, such as, but not limited to, the topics listed below are welcome.

A. Development and improvement of methods for the expression, solubilization, and purification of milligram quantities of

regulatory, cellular, and membrane associated proteins, as well as for the preparation of specifically labeled macromolecules and the recovery of proteins from inclusion bodies.

- B. Development of novel ligands, inhibitors, and other probes for spectroscopic and microscopic analysis of cellular assemblies, macromolecules and components, their localization and function in vivo and at a single molecule level.
- C. Development of instrumentation, devices, and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.
- D. Development of new methods and materials directed toward the solution of biological macromolecule structures by, but not limited to, x-ray diffraction, electron diffraction, and NMR spectroscopy.
  - 1. New methods for the determination of the structures of membrane associated proteins.
  - 2. New methods for the determination of macromolecular structures in a high throughput mode, including improved detectors, data collection, automated data analysis, and faster software for structure calculations and comparisons.
  - 3. New methods designed to improve the efficiency of beam line use at synchrotrons.
- E. Development of instrumentation for the imaging of biologically important molecules and cellular components, including but not limited to:
  - 1. Instrumentation and software for light microscopy.
  - 2. Instrumentation and software for conventional and cryo-electron microscopy, including automated apparatus for controlled and reproducible specimen preparation.
  - 3. Instrumentation, methods and technologies for analysis and manipulation of cells and subcellular components including atomic force microscopy, atomic forceps and tweezers, and solid state (lensless) microscopy.

4. Instrumentation, methods, technologies, and probes for spectroscopy, including magnetic resonance, fluorescence spectroscopy, and EPR.
- F. Bioinformatics, including but not limited to:
1. Development of databases relative to structural and cellular biology.
  2. Development of methods for linking the information that might be contained in such databases.
  3. Development of new tools that might be used for “mining” the information contained in such databases.
- G. Theoretical methods for, but not limited to:
1. The analysis of macromolecular structures.
  2. The prediction of the three dimensional structures of biological macromolecules.
  3. Improved methods for structure-based drug design.
  4. Improved methods for understanding complex systems at the cellular and organism level.
- H. The development of computerized tools that might be used in the presentation of the concepts of cell and structural biology to audiences at a variety of levels.
- B. Improvement of methodology for oligonucleotide synthesis.
  - C. Improvement in procedures for the separation and analysis of nucleic acids and proteins as these relate to genetic problems.
  - D. Improvement of methodology (technology) for genetic analysis (e.g., gene libraries, cloning techniques, probes).
  - E. Development of probes for detection of human genetic polymorphisms, including disease genes.
  - F. Development of improved procedures for cytogenetics.
  - G. Improvement in procedures (statistical, computational, laboratory) for the analysis of gene flow and gene dynamics in human populations.
  - H. Development of improved vectors for gene transfer.
  - I. Development of valid animal models for genetic diseases.
  - J. Development of quantitative approaches to the analysis of complex biological systems.
  - K. Development of new tools and models for study of the genetic architecture of complex phenotypes.

#### **Division of Genetics and Developmental Biology**

Research on developing a better understanding of fundamental processes and mechanisms of development and inheritance in health and disease. Support of basic topics in genetics and developmental biology, including nucleic acid chemistry, the structure of genetic material, the mechanisms of transmission and expression of genetic information, cellular regulation of growth and differentiation, molecular immunology, and population genetics. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of computer software for the analysis of the primary and secondary structures of nucleic acids as these relate to genetic problems.

#### **Division of Pharmacology, Physiology, and Biological Chemistry**

Research related to the actions of therapeutics, including anesthetics, and the development of biotechnological methods for their production and investigation. Research on pain management as it relates to anesthesia and the perioperative period. Research on responses to traumatic injury, including burn injury, and methods to mitigate these responses. Research leading to new knowledge of physiological functions at the molecular, cellular, and organ systems levels. Research on the structure, function, and biosynthesis of cellular components and cellular metabolism, bioenergetics, and mechanisms of enzyme action, regulation, and inhibition. Research leading to the synthesis of new materials or development of new chemical methods to probe biological phenomena or to alter the behavior of biological systems. Examples include, but are not limited to:

- A. Methods for isolation, characterization, and production of natural and bio-engineered products.
  1. Metabolic engineering for the production of biochemicals through genetic and bioengineering manipulation of biosynthetic pathways.
  2. Biosensors for use both in vivo and in vitro in process engineering.
- B. Development of innovative synthetic chemistry.
  1. Catalytic asymmetric methods and methods for large-scale synthesis.
  2. New methods applicable to combinatorial library construction, design, analysis, and/or handling.
  3. Improved methods for preparation of isotopically labeled amino acids, peptides, proteins, and prosthetic groups, and therapeutic agents.
- C. Development of enzymes, catalytic antibodies, ribozymes, artificial enzymes, and host molecules as drugs or synthetic tools.
  1. Synthesis of suicide substrates, affinity labeling agents, and transition state analogs as potential therapeutic agents.
  2. New enzyme assays to reduce the reliance on radio-isotopes.
  3. General approaches for high throughput screening.
- D. Isolation, characterization, and development of factors involved in tissue repair and wound healing, i.e., growth factors. Tissue engineering. Development of artificial skin and skin replacements.
- E. Improved systems for collection, processing, and analysis of real time physiological data from injured or critically ill patients. Application of artificial intelligence or fuzzy logic and other methods to model non-linear behavior in critically ill patients.
- F. Systems to utilize virtual reality for surgical education and remote surgical applications.
- G. Research to improve drug design.
  1. Methods for understanding of structure-activity relationships.
  2. Mechanisms of drug-receptor interactions.
  3. Development of pro-drug and drug delivery strategies.
  4. Development of molecular diversity libraries.
- H. Research to improve drug bioavailability by improved understanding of factors that influence absorption, metabolism, transport, or clearance of therapeutics and underlying mechanisms.
  1. Determination of structure-activity relationships for drug metabolizing enzymes.
  2. Determination of structure-transport relationships for active and passive transport of drugs and metabolites.
  3. Research on drug transporter structure, function, and regulation.
  4. Development and validation of models for prediction of drug bioavailability and metabolism in humans.
  5. Research on inter- and intra-individual differences in bioavailability.
  6. Methods to improve sensitivity, accuracy, speed, and simplicity for measurements of drugs and their metabolites in complex biological matrices.
- I. Application of pharmacokinetic and pharmaceutical principles to the study of large biomolecules, such as proteins, polypeptides, and oligonucleotides.
- J. Development of novel targeted delivery systems for both conventional drugs and large molecules.
- K. Research to discover, detect, and understand the genetic basis of interindividual differences in drug responses.
  1. Identification of human polymorphisms in drug receptor and drug metabolizing enzymes.
  2. Methods for pharmacogenetic and pharmacogenomic analyses and their application to phenotypic and genotypic characterization of populations.

3. Development of appropriate databases, specimen, and cell culture collections to support research in this area.
- L. Development of methods for quantitating protein and lipid glycoconjugates and for determining their structures. Development of generally applicable methods for the synthesis of branched chain oligosaccharides.
- M. Development and application of methods and materials for the elucidation of membrane protein structures at or near atomic resolution.
  1. Novel vector and host cell systems for over-expression of membrane proteins, in both unlabeled and isotopically labeled forms.
  2. Novel and high purity detergents and non-detergent solubilization agents for the purification and crystallization of membrane proteins.
  3. Apparatus to facilitate crystallization and manipulation of fragile crystals for data collection.
  4. Reagents for heavy atom derivatization of membrane protein crystals.
- N. Development of high-throughput methods for sequencing and resequencing of mitochondrial genes and nuclear genes relevant to mitochondrial function.
- O. Development of new metal ion chelators and other tools to probe and/or alter the localization and concentration of metal ions in cells and in whole organisms. Research to exploit metal metabolism and metal-regulated cellular control and cell-cell signaling processes to probe and/or alter cell function. Research to develop investigational and therapeutic applications of metal-complexes and to understand the factors governing their pharmacology and toxicology.
- P. Development of research tools to promote scientific collaboration in any of the above areas of research. For example, applications software for secure peer to peer networking to facilitate the exchange of scientific data and research materials or to construct a searchable distributed database.

## Other Research Topic(s) Within Mission of Institute

For additional information on research topics, contact:

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## NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

The NHLBI plans, conducts and supports research, clinical trials and demonstrations relating to the causes, prevention, diagnosis and treatment of heart, blood vessel, lung, and blood diseases and sleep disorders. The NHLBI SBIR/STTR program fosters basic, applied, and clinical research on all product and service development related to the mission of the NHLBI. Research may be targeted to gender, race, or age subgroups.

For more specific information about areas of interest to the NHLBI, please visit our home page at <http://www.nhlbi.nih.gov>.

Research topics of interest include, but are not limited to, research and development of the following:

## Heart and Vascular Diseases

The Division of Heart and Vascular Diseases plans and directs the NHLBI's research grant, contract, and training programs in heart and vascular diseases. These programs encompass institute- and investigator-initiated basic research, targeted research, specialized centers and clinical trials. The DHVD maintains surveillance over developments in its program areas and assesses the national need for research on the causes, prevention, diagnosis, and treatment of cardiovascular disease. The DHVD ensures that effective new techniques, treatments and strategies resulting from medical research are transferred to the community through professional, patient, and public education programs in a timely manner.

The Division has three major programs: the Heart Research Program, the Vascular Biology Research Program, and the Clinical & Molecular Medicine Program, in addition to a Research Training and Special Programs Group.

*Heart Research Program.* Supports basic, applied, and clinical research in cardiac diseases, from embryonic life to adulthood.

*Vascular Biology Research Program.* Supports research in atherosclerosis, hypertension, basic vascular biology and gene therapy for the prevention and/or treatment of vascular diseases.

*Clinical & Molecular Medicine Program.* Supports clinical, basic and engineering research on cardiovascular disease and health. Its scope includes genetic, genomic and proteomic research; engineering theory and practice applied to biology and medicine including therapeutic cardiovascular devices and diagnostic instrumentation; informatics and simulation; and cohort, case-control, and randomized clinical trials.

- A. Ambulatory monitoring (long term) of blood pressure.
- B. Angioscopes with increased flexibility and enhanced resolution.
- C. Animal models for assessing genetic determinants.
- D. Anti-hypertensive drugs from natural and synthetic sources.
- E. Biological, chemical, and mechanical sensors

- F. Biologics.
- G. Biomaterials.
- H. Biomimetics.
- I. Biotechnologies.
- J. Cholesterol measurement (total, HDL, and LDL) in fresh human serum, without matrix effects.
- K. Circulatory support systems.
  - 1. Artificial heart.
  - 2. Ventricular assistance.
  - 3. Automatic control.
  - 4. New animal models for in vivo testing.
  - 5. Percutaneous and transcutaneous transmission of electrical energy.
  - 6. Implantable rechargeable batteries and alternate power sources.
- L. Computerized modeling of hemodynamics in complex congenital heart disease.
- M. Cryopreservation of rat embryos for cardiovascular research.
- N. Development of new and improved antisense agents for the cardiovascular system focusing on the mode of introduction; the optimal length and specificity of the oligomer; non-specific interactions with other cellular components; and the potential toxic effects and the exact mechanism of the antisense oligomer.
- O. Development of phenotypic screening methods in the mouse for heart, lung, and blood diseases and sleep disorders.
- P. Diagnostic instrumentation for the mouse and rat.
- Q. Education and video systems.
- R. Functional tissue engineering.
- S. Gene and gene product relationship, structure, and function.
- T. Gene assessment and diagnostic technologies.
- U. Genomic applications and tools.
- V. Geographic sensing systems for high risk patients.
- W. Heart failure, early detection and treatment strategies.
- X. Informatics, modeling and simulation.

- Y. Intermediate phenotypes in hypertension.
- Z. Luminescent dyes to measure toxic metabolic intermediates in living cells in real time.
- AA. Mathematical and computer modeling of structure, function, and electrical activity of the normal and diseased heart.
- BB. Medical imaging systems.
- CC. Medical implants (heart valves, vascular grafts, stents, pacemakers, defibrillators, etc.).
  1. Novel designs and materials.
  2. Failure prediction/analysis.
  3. Manufacturing.
  4. Monitoring.
  5. Preservation methods.
  6. Quality assurance and quality control.
  7. Reference biomaterials for evaluation of biocompatibility.
  8. Reliability.
  9. Biological response.
- DD. Molecular and gene imaging
- EE. Neuro-imaging in hypertension.
- FF. Noninvasive methods of detecting cardiac rejection, particularly in infants and young children.
- GG. Non-toxic and selective molecular cages for delivering short-lived vasoactive agents to the vasculature.
- HH. Nutrition.
- II. Precursors of preeclampsia, pregnancy-induced hypertension.
- JJ. Preservations methods for cardiovascular tissues or organs for use in transplantation and in research studies.
- KK. Pro- and anti-angiogenic and vasculogenic genes, proteins and drugs.
- LL. Proteomics.
- MM. Radiologic phantoms mimicking the human torso.
- NN. Magnetic resonance, x-ray, nuclear medicine.
- OO. Resuscitation-enabling technologies.
- PP. Training.

- QQ. Vaccines for the prevention or treatment of atherosclerosis.
- RR. Vascular and renal tubular fluid dynamics, non-invasive assessment.
- SS. Viral and non-viral vectors for gene therapy.

## **Lung Diseases**

The NHLBI Division of Lung Diseases (DLD) maintains surveillance over developments in pulmonary research and assesses the Nation's need for research on the causes, prevention, diagnosis, and treatment of pulmonary diseases. Also within the purview of the Division are: technology development, application of research findings, and research training and career development in pulmonary diseases. The DLD plans and directs the research and training programs which encompass basic research, applied research and development, clinical investigations, clinical trials, and demonstration and education research. Two programs comprise the Division of Lung Diseases: the Airway Biology and Disease Program, and the Lung Biology and Disease Program.

*Airway Biology and Disease Program.* Focuses on basic and clinical research, education and training related to chronic obstructive pulmonary diseases, asthma, cystic fibrosis, control of breathing, bronchiolitis, respiratory neurobiology, sleep, and other adult airway diseases.

*Lung Biology and Disease Program.* Supports research, education, and training programs in lung cell and vascular biology; lung growth and development and pediatric lung disease; acute lung injury and critical care medicine; interstitial lung diseases, including pulmonary fibrosis; and AIDS and tuberculosis.

- A. Diagnostic Tools
  1. Computer algorithms for reading and comparing chest radiographs and scans (computed tomography, radioisotopes, etc.) using digitized images.
  2. Diagnose and treat respiratory abnormalities during sleep in infants, children, and adults.
  3. Imaging techniques to monitor lung cell functions in vivo.

4. Noninvasive measurement of blood gases, hemodynamics and respiratory function in infants, in children, and in adults.
  5. Noninvasive methodologies for measuring airways inflammation in asthma.
  6. Noninvasive methods to detect pulmonary thromboembolism, hypertension, and edema.
  7. Probes to monitor peripheral tissue oxygenation in vivo.
  8. Use of ambulatory monitoring techniques to diagnose and manage respiratory disorders of sleep.
  9. Use of high-resolution computerized tomography for monitoring lung function.
  10. X-ray computerized tomography to quantify pulmonary disease processes.
- B. Information and Health Education Tools
1. Computer technologies to promote adoption and implementation of asthma clinical practice guidelines in medical practice.
  2. Health education methodologies for patients, families, or communities to prevent or cope with lung diseases or to reduce their impact, especially among people with asthma who are minorities or living in poverty.
  3. Improve smoking cessation programs.
  4. Information systems to coordinate patient management and monitoring among patients and health care professionals.
  5. Interventions to reduce passive smoking in infants and children.
  6. Use of interactive and computer technology to teach self management to asthma and chronic obstructive lung disease patients.
- C. Materials and Devices
1. Blood substitutes to improve gas exchange.
  2. Emergency, portable, and servo-controlled ventilatory support devices.
  3. Improved aerosol delivery systems.
4. Improved devices for continuous oxygen administration, including airline travel.
  5. Improved extracorporeal or implantable devices for blood gas exchange (artificial lung).
  6. New approaches and technologies that can be used to engineer functional tissue, in vitro, for replacement or repair of damaged or diseased lung tissue, in vivo.
  7. Personal exposure monitors for aeroallergens and other environmental pollutants.
  8. Thrombo-resistant materials for extracorporeal or implantable devices for blood gas exchange and for indwelling catheters.
- D. Methods
1. "Clean" animal models for *Pneumocystis carinii* infections.
  2. Culture *Pneumocystis carinii* in vitro.
  3. Determine viability and enumeration of infectious *Pneumocystis carinii* organisms.
  4. Development and standardization of in vitro systems for the study of pulmonary epithelial (airway) cells and pulmonary endothelial (vascular) cells.
  5. Identification of genes causing and modifying lung diseases.
  6. Identify and detect lung cell specific differentiation markers.
  7. Identify lung stem cell types.
  8. Identify species and strain differences of *Pneumocystis carinii*.
  9. Isolate, identify, and characterize cells found in pulmonary granulomas.
  10. Methods to monitor levels of alertness or sleepiness continuously over extended periods of time.
  11. Three-dimensional static, mathematical, cell culture models of airways and alveoli to define parameters determining aeropollutant absorption, deposition, and effects.
- E. Treatments

1. Delivery of specific drugs (e.g., antioxidants, artificial proteinase inhibitors, surfactant) to the lungs for treatment of pulmonary and non-pulmonary diseases.
2. Gene therapy for cystic fibrosis, alpha1antitrypsin deficiency, primary pulmonary hypertension, and other inborn errors of metabolism affecting the lungs.
3. Improved aerosol delivery systems.
4. Novel pharmacologic and gene therapy approaches for asthma, acute lung injury, idiopathic pulmonary fibrosis, and bronchopulmonary dysplasia.
5. Novel pharmacologic approaches for treatment of sleep apnea.
6. Pharmacological means of stimulating growth and repair of alveoli and reparative or restorative elastogenesis in lungs suffering emphysematous changes.

### **Blood Diseases and Resources**

The NHLBI Division of Blood Diseases and Resources (DBDR) plans and directs an integrated research and training program, with an emphasis on non-malignant blood diseases such as Cooley's anemia, sickle cell disease, hemophilia, hemochromatosis, and disorders of hemostasis and thrombosis. A program in hematopoietic stem cell biology and transplantation focuses on use of transplantation to treat blood diseases, coordination of clinical transplant research, and identification of new research opportunities. The Division also has a major responsibility to improve the adequacy and safety of the nation's blood supply through research in transfusion medicine.

Two programs comprise the DBDR, the Blood Diseases Program, and the Blood Resources Program.

*Blood Diseases Program.* Supports research and training in nonmalignant disorders of blood cells and the hematopoietic system.

*Blood Resources Program.* Supports research and training in blood and marrow transplantation, thrombosis and hemostasis, and, transfusion medicine.

A. Animal models for blood diseases such as:

1. Fanconi anemia.
  2. Hemophilia.
  3. Hereditary hemorrhagic telangiectasia.
  4. Paroxysmal Nocturnal Hemoglobinuria.
  5. Platelet diseases.
  6. Sickle cell disease.
  7. Thalassemia.
  8. Thrombocytopenia.
  9. Thrombophilia.
  10. von Willebrand disease.
- B. Assays, especially hi-throughput technologies for:
1. Anti-thrombotic drug monitoring.
  2. Assays to detect CJD.
  3. Automated screening of therapeutic agents for sickle cell disease.
  4. Blood coagulation factor abnormalities.
  5. Blood-borne infectious agents transmitted by blood transfusion.
  6. Hematologic components of hematopoietic growth factors and cytokines.
  7. Human hematopoietic stem cells.
  8. Human leukocyte antigen (HLA) typing for stem cell transplantation.
  9. Platelet function.
  10. Predictors of autoimmune and alloimmune response.
  11. Thrombosis screening.
  12. von Willebrand disease.
- C. Drugs to Treat Hematologic Diseases and Cytopenic States
1. Anti-coagulants.
  2. Anti-platelet agents.
  3. Anti-sickling agents or other pharmacologic approaches to sickle cell disease.
  4. Anti-thrombotic agents.
  5. Fetal hemoglobin enhancing agents.
  6. Fibrinolytic and anti-fibrinolytic agents.
  7. Iron chelators.

8. Replacement agents for hematologic factor deficiencies.
9. Therapeutic uses for plasma derivatives.
- D. Equipment and procedures for the collection, separation, processing, preservation, storage, and distribution of blood and blood components.
- E. Functional tissue engineering.
- F. Gene therapy vectors and delivery systems for the treatment of hematologic genetic diseases.
- G. Health education programs to prevent or reduce the impact of blood diseases.
- H. Management and education systems for more effective and appropriate use of blood products.
- I. Methods/technologies for:
  1. In vitro inactivation or removal of microorganisms from blood, blood components, and plasma derivatives.
  2. Isolation, purification, expansion, and storage of hematopoietic stem cells.
  3. Methods/instrumentation for continuous, real-time measurement of blood flow or stasis.
  4. Measuring iron non-invasively.
  5. Non invasive measurement of blood cell counts or other blood components.
  6. Platelet storage methods that preserve biological efficacy.
  7. Prolonging the in vivo lifetime of transfused red cells for therapeutic uses.
  8. Reducing the loss of blood in neonates to phlebotomy.
  9. Screening and prenatal diagnosis of inherited blood disorders.
  10. "Silencing" the abnormal b-globin gene(s) in the hematopoietic stem cells of individuals with sickle cell disease.
  11. Synthesizing, screening, and evaluating the safety and efficacy of therapeutic oxygen carriers.
  12. Synthesizing or purifying plasma proteins for therapeutic use.
13. Techniques for improving exchange transfusions for sickle cell disease patients.
14. Testing potential anti-sickling agents.
- J. National reference laboratory to identify unusual hemoglobinopathies or coagulation disorders.
- K. Public Health Education:
  1. Computer-assisted personal interview (CAPI) for the blood donor screening process.
  2. Computerized health education programs in: blood, platelet and bone marrow donations.
  3. Tutorials for community-based providers: emerging technologies.
- L. Tools, reagents, and assays for hematologic research in mouse and other animals:
  1. Imaging devices.
  2. Micro-surgical instruments.
  3. Polyclonal and monoclonal antibodies.
  4. Recombinant and purified proteins.

## **Epidemiology and Clinical Applications**

The NHLBI Division of Epidemiology and Clinical Applications (DECA) plans and directs programs in epidemiologic studies, basic and applied behavioral research, demonstration and education research, and projects for disease prevention and health promotion, including large scale clinical trials. The research supported by the Division provides multidisciplinary approaches to heart and blood vessel, lung, and blood diseases, with a primary focus on cardiovascular disease.

DECA is comprised of two programs, the Clinical Applications and Prevention Program and the Epidemiology and Biometry Program, and the Office of Biostatistics Research.

### ***Clinical Applications and Prevention***

**Program.** Supports research into prevention of heart and vascular, pulmonary, and blood diseases through activities such as clinical trials, health promotion-disease prevention, community interventions, health education research, nutrition research, and behavioral medicine.

### ***Epidemiology and Biometry Program***

Supports and conducts epidemiological studies of heart and vascular, lung, and blood diseases in defined populations in the United States and other countries.

- A. Clinical research/intervention studies designed to improve cardiovascular disease outcomes.
- B. Clinical trial methodologies.
- C. Communication techniques for minority and low-income populations.
- D. Community and demonstration programs.
- E. Cardiovascular disease information, education, and prevention systems for primary caregivers.
- F. Interactive databases.
- G. Measures of patient adherence/compliance.
- H. Methods for:
  - 1. Lifestyle intervention.
  - 2. Matching patients to lifestyle, intervention, or treatment.
- I. Models of behavior modification
- J. New agents or treatment strategies.
- K. New assay systems/techniques to measure patient responses.
- L. New materials and equipment for enhanced medical imaging systems.
- M. New methods for communication of research results.
- N. Novel/Unique methods for collection, transmission, management and analysis of clinical data.
- O. Nutrition, physical activity, smoking, and tobacco cessation interventions.
- P. Nutrition and physical activity measurement methods.
- Q. Pharmaceutical development and toxicologic evaluation.
- R. Population tracking mechanisms.
- S. Psychosocial measurement instruments, especially in minority populations.
- T. Prognostic assays.
- U. Quality of life measurement and analytic methods.

- V. Software for:
  - 1. Clinical trials.
  - 2. Epidemiology studies.
  - 3. Literature abstracting.
  - 4. Meta-analysis
  - 5. Statistical analysis.
- W. Screening, assessment, and tracking tools.
- X. Survey questionnaires.
- Y. Training techniques and modules.

### **Other Research Topic(s) Within the Mission of Institute**

For additional information on research topics, contact:

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## **NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)**

The Human Genome Project (HGP) is an international initiative involving the NIH and several other federal, private, and international organizations. At the NIH, the NHGRI is the lead institute for the HGP. Many of the initial goals of this project--genetic and physical maps of the mouse and human, and the DNA sequences of *E. coli*, *S. cerevisiae*, *C. elegans* and *D. melanogaster*--have been realized. A working draft version of at least 90% of the euchromatic part of the human genome was completed in 2000, and the complete high quality human sequence will follow within the next couple of years. More than 25% of the human genome sequence has been finished, including all of chromosomes 21 and 22. Mouse genome sequencing has also begun; an intermediate version will be generated within the next year and the complete sequence will follow by 2004 or sooner.

Once the DNA sequence of an organism becomes available, many new avenues to studying its biology are opened. However, new and improved research tools, approaches, and capabilities are needed to discover and use the vast amount of biological information in complete genomic DNA sequences. In 1998, a set of new goals was adopted for the U.S. Human Genome Program (see Goals at <http://www.nhgri.nih.gov/98plan/>). In addition to completing the human and mouse maps and sequences, the aim of the HGP was extended to developing new technological approaches that will be necessary to understand and use genomic DNA sequence. Therefore, important areas of attention for the NHGRI will be the continued development of new technology for mapping and sequencing, for the interpretation of genomic sequence, including functional

analysis of non-coding sequences, for the study of sequence variation, and for the analysis of gene expression. Support for scholarly research as the foundation for understanding the ethical, legal and social implications (ELSI) of genomics and genetics research will also continue to be a major area of emphasis.

The success of the Human Genome Project has been due to the development of improved technologies, strategies and methods that can be applied on a genome-wide scale in a cost-effective manner. As part of its interest in continuing to provide support for technology development research and, therefore, the NHGRI solicits SBIR/STTR grant applications in the areas listed below. Innovative approaches in other areas not listed in the major topics below will also be seriously considered.

### **DNA Sequencing**

Development of (1) innovative technologies and strategies that promise to reduce the cost, increase the throughput, or improve the accuracy of large-scale DNA sequencing of complex genomes; (2) strategies and technologies for obtaining DNA sequence in the gaps that are left by current sequencing methods or that will improve the efficiency of sequencing in genomic regions that have proved difficult to sequence due to limitations in available cloning and sequencing technology; (3) innovative sequencing technologies and strategies for SNP detection; and (4) instrumentation and methods development, from technical feasibility through prototype development and introduction into production.

### **Human Genome Sequence Variation**

Development of new or improved methods and analytic tools for: (1) the large-scale identification, scoring, and interpretation of DNA sequence variants; (2) the identification of haplotypes; and (3) facilitation of studies relating the distribution of variation to population history in order to determine the density of SNPs or other markers needed for gene mapping.

### **Comparative Genomics**

Improvement in the technology for generating clone libraries useful for genomic analysis with DNA inserts that are stable, free of artifacts, and faithfully representative of genomic DNA

from complex organisms. Generation of (1) clone libraries of additional commonly used mouse strains; (2) mapping resources for the mouse; (3) a low resolution (5cM) single nucleotide polymorphism (SNP) map to determine the usefulness of this resource for studying complex diseases in the mouse; and (4) genetic maps of additional commonly used mouse strains using single sequence length polymorphisms as markers.

### **Functional Genomics**

(1) Development of new or improved technologies for large-scale or genome-wide approaches relating to: gene discovery, full-length cDNA synthesis, or gene expression analysis; (2) analysis of protein-ligand interactions, such as protein-protein interactions; protein modifications; (3) functional analyses of non-coding sequences; and (4) generation and detection of mutations.

### **Bioinformatics and Computational Biology**

Development of new or improved tools for: (1) obtaining, representing, analyzing and archiving data and (2) improving databases, in the areas of DNA sequence, gene mapping, complex trait analysis, genetic variation and homology, and functional genomics.

### **Ethical, Legal and Social Implications (ELSI) of Genomics and Genetics Research**

Examination of: (1) the issues surrounding the completion of the human DNA sequence and the study of human sequence variation raised by the integration of genetic technologies and information into health care and public health activities and (2) the integration of knowledge about genomics and gene-environment interactions into non-clinical settings.

### **Other Research Topic(s) Within Mission of Institute**

Individuals interested in any of the above listed areas are encouraged to contact the NHGRI staff listed below. For more specific information about areas of interest to the NHGRI, please visit our home page at [http://www.nhgri.nih.gov/Grant\\_info](http://www.nhgri.nih.gov/Grant_info).

For additional information on research topics, contact:

For all research topics except ELSI

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### **NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)**

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro-AIDS research). Ultimately, this research will lead to greater understanding, better treatment and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through scientific communications and public education, and in its more effective implementation in practice and service delivery systems. There is a general need to develop reliable and inexpensive equipment, and other products, that can serve these needs.

For additional information about areas of interest to the NIMH, please visit our home page at <http://www.nimh.nih.gov>.

### **Division of Neuroscience and Basic Behavioral Science**

Through research in neuroscience and basic behavioral science we can gain an understanding of the fundamental mechanisms underlying thought, emotion, and behavior and an understanding of what goes wrong in the

brain in mental illness. Research sponsored by the Division of Neuroscience and Basic Behavioral Science covers a broad range of neuroscience topics: from both experimental and theoretical approaches, from molecules to whole brains to populations of individuals, from single cell organisms to humans, from across the entire lifespan, and from states of health and disease. This division also supports research on the basic behavioral, psychological, and social processes that underlie normal behavioral functioning. The topics listed below reflect the NIMH interest in technologies related to this broad range, but should not be considered to be a complete list. Prospective applicants are strongly encouraged to contact Dr. Michael Huerta (listed below) with questions about the relevance of their interests to the mission of this division.

A. *Cutting-Edge Technologies for Neuroscience Research.* Most of the research topics listed after this one are posed from the Division's neuroscience and basic behavioral science mission-oriented perspective, however, the technologies that might be developed to address those mission goals might be quite fundamental. Prospective applicants familiar with such technologies, but not familiar with the mission-related use of these technologies, are strongly encouraged to contact Dr. Michael Huerta (listed below) for assistance in bridging this gap between their technical knowledge and knowledge of the neuroscience-related mission of NIMH. Technologies and approaches that might be used in products relevant to this mission include, but are not limited to:

1. Caged molecules. These could be activated, or release an active agent, when specified bonds are broken by chemical, biochemical, photic, or other means. Among other uses, such molecules could be used to indicate biochemical or physiological processes or to deliver pharmacologic substances to highly localized brain regions.
2. Genetically engineered proteins. Such proteins could be put to any number of uses, including to express a fluorophore or chromophore at the occurrence of specific biochemical processes to report the time and location of such processes in brain tissue.

3. Inducible gene expression. Methods to turn on or off expression of particular genes in transgenic animals on the basis of time in the lifespan, location in the brain, or other factors. Such a capability would significantly advance basic brain research, and would have important implications for treatment and therapy of mental illness.
4. Combinatorial approaches. These are high-through-put approaches that can be used to screen and synthesize molecules that affect brain cells.
5. Biosilicon devices. These couple biological molecules with semiconductor materials and technologies, and could serve as biosensors for endogenous molecules (specific nucleotide sequences, proteins, etc.) or for exogenous substances (or their metabolites). Among other uses, these could be employed in monitoring biological processes or drug levels in patients.
6. Biocompatible biomaterials. Such research and development relates to the chronic use of electrodes and other probes used in brain research, as well as implanted drug delivery devices.
7. Nanotechnologies. This emerging area of technology presents a wide range of opportunities for brain research, from the fabrication of probes to monitor brain physiology to novel means of delivering drugs and other substances.
8. Acousto-optics and opto-electronics. These technologies offer innovative and versatile ways of interacting with optical elements in imaging instruments. Such technologies could, for example, be used in fluorescence microscopy.
9. Imaging technologies. At both macroscopic and microscopic levels, including non-optical scanning, tunneling and force technologies for imaging at subcellular and molecular levels.
10. Informatics tools. Such technologies allow brain scientists, clinicians and theorists to make better sense and use of their data. These tools and approaches include those to acquire,

store, visualize, analyze, integrate, synthesize and share data, including those for electronic collaboration.

11. Simulation technologies. Computer-based simulations of parts of neurons, neurons, circuits or even organisms to observe the manner in which these components interact. For example, simulations of individual organisms with constellations of particular traits that vary across individuals would allow analysis of their interactions and their impact on the population as a whole.
  12. Mathematical and computer algorithms. Such algorithms could be used to analyze large and/or complex data sets. Among other applications, these could be used to segment images (obtained from electron or light microscopes, or from volumetric imaging instruments such as confocal microscopes and magnetic resonance imagers), filter noise, visualize data or search vast data sets for specified patterns or data (e.g., use of pattern recognition algorithms to search time series data sets obtained from electrophysiological recording of neural activity, or video data obtained from behavioral analysis of genetically altered animals).
  13. Telemetry. Transferring data from one point to another is important for neuroscientists monitoring the physiological signals from the brain. Telemetry, even over relatively short distances (from a few millimeters to a few meters), could, for example, provide a means to obtain data from awake, behaving animals without interfering with the behavior of interest.
  14. Biosensors. Neurons communicate with each other through thousands of different chemical substances; internally, molecular pathways direct the function of the neuron. Sensors of high specificity and sensitivity for such substances would provide neuroscientists with important new ways to study the brain.
- B. Instrumentation for Basic and Clinical Neuroscience Research. Modern equipment that uses the most recent technological advances is needed in

neuroscience research so that neural substrates of mental illness can be identified and localized. The NIMH is interested in supporting research and development of new or improved approaches relevant to, but not limited to, the following:

1. Mass spectrometry (new quantitation, better detection in complex mixtures, etc.).
  2. Neurophysiology (microelectrodes, smart nanoscaffolds, macroelectrodes, biocompatible coatings, interfaces to electronics, software for data analysis, visualization, etc.).
  3. Two or higher dimensional electrophoresis (increased sensitivity and ease of use, software for analyzing data, etc.).
  4. Cell sorting (based on cell size, type, function, etc.).
  5. In vivo electrochemical voltammetry (more sensitive and selective electrodes, software for data analysis, etc.).
  6. High performance liquid chromatography (improved reliability, specificity, sensitivity, etc.).
  7. Physiological and behavioral monitoring (temperature, activity, sleep duration, neuronal activity, EEG activity, EKG, pulse rate, recording, capture and analysis of multiple single unit activity from microelectrodes).
  8. Associated software.
- C. Macroscopic Neuroimaging. Modern technologies allow for the observation of the structure and function of the intact brain. This capability has the potential to greatly advance understanding of the brain in both health and disease, and across the lifespan. NIMH is interested in advancing this area of technology through enhancing current tools and approaches, as well as developing entirely new ways to image the brain. All modalities are of interest, including, but not limited to: magnetic resonance imaging (MRI) or spectroscopy, positron emission tomography (PET), optical imaging or spectroscopy, single photon emission computed tomography, etc. Due to its greatly increased use in

recent years, technologies specifically focused on improving the utility of fMRI techniques are of particular interest.

1. Innovative agents and/or technologies to visualize brain connectivity in situ with minimal invasion.
2. Improvement in the techniques, the design and construction of devices for non-invasive imaging for any modality, for example, improving spatial resolution, quantitative accuracy, signal-to-noise ratio, and electronics.
3. Development and enhancement of non-invasive imaging techniques for evaluating alterations in brain physiology produced by drugs. These would include techniques for monitoring changes in regional blood flow; concentrations of tissue metabolites; and the distribution and activity of receptors.
4. Synthesis, or isolation from natural products, of highly selective receptor ligands or indicators of neurochemical processes, which would be labeled for imaging by one or more particular modality.
5. New approaches in radiochemistry that will permit more exact identification of the chemical changes associated with behavioral states (e.g., sleep or arousal) or mental illness as observed with any particular neuroimaging modality.
6. Better tools and approaches for producing isotopes and other chemical agents used in neuroimaging.
7. Synthesis of molecules containing stable, rarely occurring isotopes designed to be detected by non-invasive imaging techniques (e.g., fluorine-containing molecules, carbon-13 labeled substrates).
8. Automated interface systems for handling PET radiopharmaceuticals; oxygen-15 and other isotope-based radiopharmaceuticals have limited use because of the difficulty in handling the isotope.
9. Methods and associated products for quantitation of imaging data including

new statistical approaches for evaluating the data.

10. Methods to integrate routines for greater and more precise computer enhancement of the images, and for combining or overlaying images obtained from multiple modalities.
  11. Software needed for the precise quantitation of data obtained from these imaging techniques with emphasis on the reliable definition of discrete, anatomically distinct areas within the brain.
  12. Novel agents or other tools to increase the ability to correlate features of MRI images with histological features (e.g., cytoarchitecture or chemoarchitecture) both identified and those yet to be identified.
  13. The generation of physiologic measurements from images of regional radioactivity generated during PET, especially for the study of brain neurotransmitter/neuroreceptor systems.
  14. Novel approaches to visualizing data obtained in neuroimaging, such as the computational "unfolding" of three-dimensional images of cerebral cortex.
  15. Improved methods for pediatric brain imaging. These would include: software and database products, equipment for creating a "child-friendly" environment and for the behavioral training of children and impaired subjects for cooperation and motion reduction during neuroimaging procedures.
- D. Microscopic Neuroimaging. The morphology of individual neurons and the distribution of subcellular components within them, are key to understanding the manner in which these cells function. Advances in microscopy and in the development of agents indicating neuronal structure and function that can be visualized microscopically are important to the NIMH's interest in brain research. This includes novel devices and approaches (single and multi-photon, tunneling, confocal, etc.); enhancements of current technologies, agents and ligands to be imaged (agents indicating specific biochemical processes or structures, etc.);

software to assist interaction with the instrument or data; and other related technologies and methods. Examples would include, but not be limited to:

1. Methods to boost signal to noise ratios in images obtained by microscopes.
2. Software and hardware for analyzing image data obtained by microscopes, including tools to automatically or semi-automatically: identify particular profiles (e.g., labeled cell bodies), segment images, reconstruct images into three dimensional representations, perform unbiased counting and measuring, etc.
3. New approaches to performing spectral analyses of data obtained through microscopy.

E. *Molecular and Cellular Neurobiology and Neurochemistry*. Manipulating and studying basic molecular, cellular and chemical processes has led to insight to understanding brain function, and has provided the foundation on which pharmacological interventions have been developed for the treatment of mental illness. NIMH is interested in supporting a wide range of new techniques and tools related to this area. These include, but are not limited to:

1. New low-cost techniques for hybridoma production of monoclonal antibodies specific for "neural antigens" (e.g., neurotransmitters, small peptides, neurotransmitter receptors).
2. Innovative methods for establishing a "monoclonal bank" (frozen cells) for each of the cell lines as a permanent, widely available, reliable, and low cost source of monoclonal antibodies for research on the nervous system.
3. Labeled antibodies or other agents that will readily identify receptors for which there are no ligands (orphan receptors) and which have low densities in the brain.
4. Automated methods for quantitating the low levels of bound ligands for quantitating receptors that are sparsely scattered in the brain.

5. New techniques for low-cost production of large quantities (e.g., 100 gram scale) of useful cell lines.
6. New cell lines that express each of the known neurotransmitter receptors so that each cell line will be homogeneous for one receptor.
7. New cell lines that express each of the above receptors linked to some metabolic function and/or second messenger so that the functional consequences of receptor occupancy can be detected.
8. High volume, inexpensive assay methods for measuring both receptor occupancy and cellular response for each of the receptor types.
9. Develop cell culture models for neurons, including methods of purifying homogeneous populations of non-transformed cells by, for example, developing markers to identify neuronal cell types for use in characterizing cell-type-specific signaling pathways which may be useful in tracking the effects of various drugs.
10. Develop techniques for either activating or deactivating specific ion channels, receptors and signal transduction pathways.
11. Develop dynamic biochemical and imaging assays that allow measurement of variables now obtained only through electrophysiological techniques.
12. New approaches to study the multiple functions of particular proteins.
13. Tools to study post-translational changes in proteins in specified tissue compartments.
14. Technologies to study functional entities within cells (e.g., green fluorescent protein approaches).
15. Tools and approaches to study coordinate changes in genes and their functional relationship to phenotypes, including phenotypes associated with specific brain disorders.
16. New ways to assess quantitatively transcription of genes in real time in a manner that is minimally injurious to

cells (e.g., non-permeabilizing approaches).

17. Novel tools and approaches to study protein-protein interactions, especially those with phosphoproteins.

F. Genetic and Transgenic Technology.

Advances in genetic and transgenic technologies offer many opportunities to probe fundamental questions about the brain, behavior and pathology. NIMH is broadly interested in these areas; some examples of topics relevant to the mission of this Institute include, but are not limited to:

1. Methods to perform site-directed mutagenesis in cell lines for the study of membrane proteins such as ion channels and neurotransmitter receptors.
2. Development of gene “knockout” or “knockin” animals using such approaches as homologous recombination targeting genes important in neurotransmission, development, and tropic interactions as well as in generating behavioral models of disease.
3. New methods to delete or alter targeted genes in the preparation of transgenic animals including methods that increase or decrease gene expression.
4. Development of new techniques and apparatus for delivery of antisense oligonucleotides into cells and specific tissue such as the brain.
5. Develop standardized behavioral tests to assess the gene knockouts and/or gene “knockins” affecting neurotransmission.
6. New approaches for cell-specific, tissue-specific, age-specific, transient gene activation and/or inactivation.
7. Innovative technologies to study gene function and expression.
8. Development of embryonic stem (ES) cell lines from rodent strains (rats and mice) of relevance to behavioral research.
9. Development of technologies and approaches to facilitate the collection

and distribution of ES cell lines containing mutations of potential relevance to behavioral research.

10. Develop methods for long-term storage of transgenic germ cell lines.
11. Develop technologies and approaches to aid in the renewal of founder colonies of transgenic mice from repositories of transgenic germ cell lines.
12. Develop databases on neurobiological transgenic animals produced to date, including information such as the origin of the transgenic animal, key features of the biological and behavioral mutant, availability and location of germ cell lines, and existence of breeding colonies.
13. Develop gene transfer technologies such as viral vectors to produce long-term, stable gene expression in the brain.

G. Neuroimmunology. Research on the interplay between the brain, neuroendocrine system, and, immune system has revealed important links between these major homeostatic system components. Examples of NIMH-relevant topics in this area include, but are not limited to:

1. Development of new tools to explore the special properties of the blood-brain barrier responsible for the selective delivery or retention of cytokines, immune cells, and drugs affecting immune activity in the brain.
2. Development of assays for identifying potential autoimmune components of psychiatric disorders (other than the usual screening for “markers”).
3. Identification of critical molecules, processes, and pathways mediating signals from the peripheral immune system to the brain.
4. Development of novel cytokine ligands and antagonists.

H. Pharmacology. Pharmacological intervention represents a major force in the treatment of mental illness, and NIMH is interested in supporting research and development in this area. Relevant topics include, but are not limited to:

1. New chemical entities with high, selective affinities for each of the receptors in the brain.
  2. Methods to evaluate old and new chemical entities (including complex mixtures of crude extracts from natural products) for possible therapeutic usefulness using "in vitro" and "in vivo" assays and model systems.
  3. Methods for extraction, fractionalization, and isolation of active compounds from natural products. Water-soluble compounds are of particular interest due to the difficulty of the procedures.
  4. Computer algorithms that model receptors to evaluate theoretical permutations of known molecules to find the molecule with the maximum probability of having the highest affinity for a specific receptor as well as those that have the potential for the most desirable "on" and "off" rates.
  5. Computer models of the blood brain barrier and evaluate potential and actual drug molecules for their ability to cross or penetrate this barrier.
  6. Development of new animal tests/behavior with potential value for evaluating psychotherapeutic properties of drugs.
  7. Strategies for evaluating pharmacological agents (e.g., animal behavioral testing, computer simulation) on cognitive function.
  8. Behavioral "models" similar in animals and humans; behavioral pharmacological effects that may serve as "surrogate" markers in humans.
  9. Development of novel drug delivery systems.
  10. Tools for Drug Development including neuroimaging (e.g., radiolabeled compounds) and development of animal models.
  11. Pharmacological profiling (in vitro and in vivo) for potential therapeutic drugs.
  12. Methods for evaluation of long-term effects of psychotropic drug administration.
  13. Improving existing, and developing new, vectors for delivery of genes to the brain.
  14. Development of novel therapeutic approaches based on drug-induced changes in gene promoter activity.
- I. Tract Tracing Methods and Tools. Little is known about the details of the connectivity of the human nervous system, because the best tract tracing techniques are invasive and require the deposit of substances in vivo. Methods that would be applicable to post-mortem tissue would allow significant progress in connectional studies of human tissue, as well as non-human tissue, particularly with regard to the development of connections and the connections of structures not easily accessed in vivo.
- J. Basic Behavioral Science. It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.
1. Methodological research and development: There is a need to devise new ways of data collection, analysis, management and dissemination.
    - a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
    - b. Computer software to ease analysis of behavior monitored by video or telemetry systems.
    - c. Innovative computer based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.
    - d. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.
    - e. Causal modeling methodology as applied to correlational longitudinal data sets.

- f. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.
  - g. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.
  - h. There is a need for the development of hardware for time-stamped diary collecting instruments for use in actigraph studies of circadian rhythms in children and adolescents. Diaries are critical for the evaluation of activity data, and time-stamped diary collecting instruments can ensure investigators of receiving reliable information.
  - i. Web-based software tools for designing, updating, sharing, linking, and searching databases containing detailed information about the methodology and results of behavioral science studies.
2. Diagnosis and assessment of emotional and psychological states such as automated methods to detect specific emotional states using behavioral and autonomic indicators.
  3. Instrumentation and equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.
    - a. Physiological monitoring: Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:
      - i. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.
      - ii. New techniques for electrophysiological images from the level of the single cell and surface EEG recording on the scalp.
      - iii. Small, portable automated systems to monitor eye function (e.g., pupil size, accommodation) and eye movements.
      - iv. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real-time.
    - b. Measurements of infant development using physiological and behavioral measures.
      - i. Psychophysiological measures to evaluate infants during the first six months of life.
      - ii. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).
      - iii. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.
      - iv. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.
    - c. Behavior monitoring and analysis.
- K. Educational Tools. Neuroscience and basic behavioral science area compelling areas of science that not only touches upon a diverse array of disciplines, but also provides insights to the essence of what it

is to be human. Products aimed at teaching the substance of these fields to students of all ages would be useful in disseminating this information and these insights. Examples include, but are not limited to: software and other interactive media used to convey fundamental concepts about the brain to children; computer simulations of neuroscience experiments; updateable media that presents state-of-the-art information on particular topics for use by experts; website or other online, interactive electronic vehicle to allow for sharing of information about the brain and its functions, including technologies for holding interactive research conferences related to basic behavioral sciences, basic neuroscience, or clinical neuroscience.

- L. Neuroinformatics. Data generated by brain research are diverse, vast, and complex. The diversity of data is due to the fact that neuroscience data are obtained from: theoretical, experimental and clinical approaches; from levels of biological organization that span molecules to populations of individuals and from single-cell organisms to humans; and from states of health, disease, and models of disease. The quantity of data in brain research is the result of tens of thousands of neuroscience laboratories working around the world. The complexity of data reflects the high level of interconnectedness of the data, and their high dimensionality. Neuroinformatics is a new area of science that draws upon neuroscience, information science, computer science, statistics, applied mathematics, and a variety of engineering fields to develop tools that will let neuroscientists make better sense and use of their data. These tools include software and hardware for digital data acquisition, visualization, analysis, integration, and sharing (e.g., through tools for electronic scientific collaboration). Such tools can address data of any type or from any area of neuroscience; examples include, but are not limited to:

1. Databases, querying approaches, and information retrieval tools for neuroscience and neuroscience-related data.
2. Tools for neuroscience data visualization (and other forms of

presentation) and manipulation (probabilistic atlases of brain structure or function, new statistical approaches for analyzing data, etc.).

3. Software for integration and synthesis of neuroscience data (computational models of neurons to integrate data about structure and function, environments to merge data from multiple imaging modalities, etc.).
4. Tools for electronic collaboration to allow neuroscientists to interact with colleagues, data, and instruments at a distance (this could include novel types of "groupware", etc.).
5. Tools that bridge existing neuroscience and biology information tools and resources, such as databases and informatics tools associated with genome mapping efforts.

For further information on basic and clinical neuroscience or basic behavioral science research topics, contact:

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#### **Division of Mental Disorders, Behavior and AIDS**

The Division of Mental Disorders, Behavior and AIDS is responsible for planning, directing and supporting programs of research, research

training, research dissemination and resource development in behavioral science, developmental psychopathology, prevention and early intervention, and in research on the causes of and prevention of HIV (AIDS). The division is comprised of the Center for Mental Health Research on AIDS and three branches. These branches are: The Developmental Psychopathology and Prevention Research Branch; the Adult Psychopathology and Prevention Research Branch and the Health and Behavioral Science Research Branch. Their respective functions are as follows:

*The Center for Mental Health Research on AIDS.* This Center plans coordinates, and supports biomedical and behavioral research designed to develop a better understanding of the biological and behavioral causes of HIV (AIDS virus) infection, and more effective mechanisms for the diagnosis, treatment, and prevention of AIDS. The Center is also interested in identifying and addressing behavioral issues in vaccine trials and in identifying the effects of HIV infection on the central nervous system.

*Developmental Psychopathology and Prevention Research Branch.* The focus of this branch is on: risk/protective factor identification; early social, emotional and cognitive developmental processes leading to psychopathology or resilience and the translation of risk and developmental research into new prevention, early intervention and treatment strategies. Studies may address modifiable and potent individual, social, cultural and environmental factors and processes; critical dimensions of behavioral expression that confer risk such as emotion regulation, and impulse control and executive functions.

*Adult Psychopathology and Prevention Research Branch.* This branch focuses on research that reflects significant public health concerns. These include: developing preventive interventions for adult psychopathology which are based upon epidemiologic and clinical research, refining assessment and diagnosis of adult psychopathology and disability and clarifying the relations among psychological, biological, social, cultural and environmental factors involved in adult mental illness and disability.

*Health and Behavioral Science Research Branch.* This branch supports research on

general medical illnesses and behavior and their relationship to mental disorders. Emphasis is on the mechanisms and processes linking medical and mental illnesses, development and testing of early interventions, factors that influence adherence to treatment, help seeking behavior, cognitive and decision making factors that influence the choice of treatment or mental health services, stigma and services utilization.

All applications relevant to the mission of the Division of Mental Disorders, Behavior and AIDS will receive full consideration. **Possible areas for future research include:**

- A. *Instrumentation for basic, and clinical behavioral research.* Modern equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.
  1. Physiological monitoring: Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:
    - a. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.
    - b. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real-time.
  2. Measurements of infant development using physiological and behavioral measures.
    - a. Psychophysiological measures to evaluate infants during the first six months of life.
    - b. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).

- c. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.
  - d. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.
- 3. Behavior monitoring and analysis
  - a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
  - b. Computer software to ease analysis of behavior monitored by video or telemetry systems.
- B. *Behavioral science, research and development.* It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.
  - 1. Assessment tools
    - a. New technologies to assess and validate occurrence of and injuries resulting from physical and sexual abuse.
    - b. Technologies to assess CNS effects of psychosocial variables and interventions.
    - c. Methodologies to assess preoccupation with thoughts of violence or use of violence to solve perceived problems.
  - 2. Methodological research and development. There is a need to devise new ways of data collection, analysis, management and dissemination.
    - a. New relatively culture-free taxonomies and/or measures of basic behavioral and social phenomena that can be employed in research across sociocultural contexts.
- b. Innovative computer based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.
  - c. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.
  - d. Causal modeling methodology as applied to correlational longitudinal data sets.
  - e. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.
  - f. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.
  - g. Development of improved standardized instruments and methods for assessing assets, deficits, and disorders in children's social and emotional functioning that are sensitive to variations in social-environmental contexts.
  - h. Innovative methodologies for assessing continuity and change in neighborhood/community context variables.
  - i. Innovative methodologies for assessing and integrating historical neighborhood/community contextual variables with existing data sets.
- C. Health and behavior and prevention.
  - 1. Innovative, computer based methods to monitor prevention and intervention efforts and correlate them with outcome measures are needed. Results should be accessible to other interested parties without compromising the privacy of the individual. Evaluations could allow a multivariate analysis of relationships among the following:

- a. Perceptual, personality, cognitive and neuropsychobiological test data.
  - b. Verbal-linguistic characteristics.
  - c. Motor behavior and facial responses.
2. Development of innovative programs and methodologies aimed at mental disorder prevention and mental health promotion, including regular and interactive video models, especially those appropriate to minority populations.

***Science education in mental disorders, behavior and AIDS.***

There is a critical need for improvement in science education, particularly in areas specifically related to brain, behavior and mental illness.

1. Research on the best ways to present neuroscience and behavioral science information to particular groups of students (e.g., kindergarten through sixth grade; African Americans, Hispanics, persons with physical and cognitive disabilities).
2. Computer based systems to teach students how to observe scientific phenomena related to the brain, behavior and mental illness, and to report them clearly in writing.
3. Research on better ways to communicate new knowledge and directions of scientific growth in the area of neuroscience and mental illness to teachers and curriculum developers.

***Diagnosis and assessment of emotional and psychological states.***

1. Automated methods to detect specific emotional states using behavioral and autonomic indicators.
2. Development of techniques for maintaining or restoring mental capacities in older adults who experience declining learning and memory abilities due to age-related brain disorders.
3. Development of behavioral and laboratory aids to establish diagnoses

for mood, anxiety, and other psychiatric disorders.

4. Development of standardized and valid instruments to assess exposure to traumatic events and victimization experiences as well as the physical and mental health consequences of such exposure.

***D. Knowledge transfer.***

1. Computerized, internet-based data storage, analysis, and retrieval systems to provide professionals and the general public with current information on mental disorders and behavioral dysfunctions and their prevention and treatment.
2. Systematic approaches to the dissemination of the latest clinically-relevant NIMH-supported research findings to relevant populations of service providers, advocacy groups, client groups, and policy makers, e.g., by means of targeted research summaries, recruited list serves, or other print or electronic communication.

***NIMH Center for Mental Health Research on AIDS***

The NIMH office on AIDS Research supports research on the effects of HIV on the central nervous system and on developing effective HIV prevention and risk reduction interventions. Examples of possible SBIR initiatives include:

- A. Behavior Change and Prevention Strategies to reduce HIV transmission especially among minority populations and hard to reach subsets of those populations.
  1. Development of methods to reduce, prevent and/or change HIV-associated and STD risk behaviors.
  2. Development of relapse prevention methods for HIV-associated risk behaviors.
  3. Development of curricula for training clinicians and other health care practitioners in the prevention and treatment of HIV-related mental disorders.
  4. Development of school-based curricula to promote HIV prevention by educators and teachers.

5. Development of HIV prevention materials to be used in community-based outreach programs for special populations (school dropouts, homeless, street youth, incarcerated youth).
  6. Development of curricula for training in multicultural issues and development of cultural competence in HIV risk assessment, counseling, and prevention.
  7. Development of print and/or computer based materials to assist primary care practitioners in informing their patients about HIV risk and prevention.
- B. Neuro-AIDS: HIV-1 Infection and the Nervous System
1. Development of non-invasive methods for detecting and quantitating HIV within the CNS.
  2. Development of in vivo or in vitro models to identify mechanisms underlying CNS dysfunction resulting from HIV infection.
  3. Development of novel compounds to block or reverse CNS dysfunction associated with HIV infection.
  4. Development of agents to block HIV entry into the CNS.
- C. AIDS Mental Health Services Delivery
1. Video and computer-assisted methods to train health and mental health care providers in the psychosocial and neuropsychiatric aspects of HIV infection and AIDS.
  2. Development of methods to assess functioning in families in which there is an HIV infection in order to develop improved treatment modalities.
  3. Development of novel programs to train people infected with HIV in self-care management and identification of stress and development of improved coping strategies in order to improve quality of life.
  4. Development of novel programs to help people recognize and seek treatment of mental health problems arising from living with HIV/AIDS as a long-term chronic condition.

5. Development of information, instruments or methodologies to improve and/or track adherence to complex HIV/AIDS drug therapies for Hispanic and African American populations.
6. Development of innovative approaches to link researchers with community providers in the implementation of research-based HIV prevention efforts at the community level.

For further information on mental disorders, behavior, or AIDS research topics, contact:

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### **Division of Services and Intervention Research**

The Division of Services and Interventions Research supports research, research demonstrations, research training, resource development, and research dissemination in prevention and treatment interventions, services research, clinical epidemiology, and diagnostic and disability assessment. The division is comprised of three branches: Services Research and Clinical Epidemiology Branch, Adult and Geriatric Treatment and Preventive Intervention Research Branch, and Child and Adolescent Treatment and Preventive Intervention Research Branch.

### **CLINICAL TRIALS, CLINICAL PRACTICE, AND EFFECTIVENESS RESEARCH**

This division is concerned with both the translation of neuroscience and behavioral science knowledge into clinical practice and with the development of research on the effectiveness of treatment and rehabilitation. This involves clinical and clinical services research on the delivery of mental health services in hospitals, clinics, communities, and in a wide variety of systems of care, e.g., managed care, primary care, etc.

- A. *Services Research and Clinical Epidemiology Branch*. This branch supports research on the organization, financing,

delivery, effectiveness, and appropriateness of mental health care in everyday settings in order to find ways to improve the effectiveness, efficiency, and equity of mental health services (including preventive services) in community and other settings. Also supported are studies on pharmacoeconomics, pharmacoepidemiology, and the distribution, determinants, and course of mental illness in the context of various clinical settings. Mental health services include mental health care provided in specialty mental health and general health care settings, including primary care, hospitals, nursing homes, and other residential care settings, as well as in educational settings and various legal system settings, such as jails, juvenile detention and correctional facilities, prisons, and probation and parole programs. Other services often needed by mentally ill persons include social services, vocational and rehabilitation services, welfare, and housing. Relevant services include those provided to children and adolescents with emotional disorders, adults and elderly adults with mental disorders, and persons with mental illness that co-occurs with physical illness and with alcohol and/or drug abuse disorder. Research methodologies include ethnographic studies, surveys, and analyses of secondary data, randomized controlled trials, quasi-experimental designs, cohort, and case-control studies.

Advances in clinical epidemiology, mental health treatment and services research fields have made it imperative that intensive work continue in the areas of assessment/screening technologies, outcome assessment measurement and measurement packages, dissemination technologies, data analysis techniques, and the training of clinicians and providers. The translation of efficacious and effective treatments into primary care, community mental health centers, and managed care settings is both a major challenge and opportunity to develop technologies and systems that will improve the care and rehabilitation of patients and enable them to profit from the research advances that have been made. Research is needed on the dissemination of empirically supported treatments or services.

1. Methodological research program. Development, testing, and refinement of methodologies and instruments to facilitate research on services for mentally ill persons, including measures of severity of illness, family burden, social support, quality of care, effectiveness of care, direct and indirect cost of mental disorders, and short-term and long-term outcome measures; studies submitted by statisticians, psychometricians, and other experts in research methodology and scientific data analysis for work on the design, measurement, and statistical challenges inherent in conducting mental health services research.
2. Outcomes and quality of care research. Tools, scales, and measures to assess differences in quality and outcomes of care in various practice types and tools to monitor outcome and quality; analyze the appropriateness of treatment including medications; development of tools and methods to assess the coordination of treatment and other care across settings and over periods of time.
3. Managed care and systems research. This program supports studies on the organization and delivery of mental health services and related services in different settings. Methods and tools are needed: to evaluate the impact of various processes of managed behavioral health care, such as utilization management, gatekeeping, and case management on access, cost, and quality; the analysis of managed care structures across sectors which promote linkage and integration between different providers; to examine ways to coordinate mental health, health, and human service systems financed by public and/or private resources to provide cost-effective care.
4. Sociocultural research program. This program is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral

sciences in general. The program supports research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services. Methods and tools are needed to assess need for clinical services, effective ways of providing culturally competent care, and assessing outcomes for persons from differing social and cultural groups.

5. Child and adolescent services research program. This program includes research on patterns of mental health service use, and the quality, organization, and financing of services for children with mental disorders and their families; services provided in multiple sectors and settings, such as schools, primary care, child welfare, juvenile justice, and mental health; service needs and delivery of services to subpopulations of youth with co-morbidities of various types; clinical and economic evaluation of innovative service models. Methods and tools to address the above areas are needed.
6. Cost and financing research. This program includes research on economic factors affecting the delivery of mental health services including the economic burden of mental illness; financing and reimbursement of public and private mental health services; impacts of alternative financing methods such as capitation, risk-adjusted contracting, and physician fee schedules on the cost of mental health care; pharmacoeconomics; evaluation of insurance coverage and various benefit designs including mandated coverage and mental health insurance parity; cost benefit, cost-effectiveness, and cost-utility analysis of mental health service interventions; market forces affecting demand for and supply of mental health care; and economic analysis of practice patterns of different mental health providers. The development of effective ways to access and use fiscal and outcome data that is often private or unavailable for research is needed. Also, statistical and methodological tools, computer software, and other analytic

approaches to address the above issues, such as cost benefit, and cost-effectiveness analyses.

7. Primary care research. This program includes studies on the delivery and effectiveness of mental health services within the general health care sector; recognition, diagnosis, management and treatment of mental and emotional problems by primary care providers; coordination of general medical care with and referrals to mental health specialists; provision of psychiatric emergency services, consultation/liaison psychiatry, and other psychiatry, psychology, and social work services within the general medical care sector; studies which improve understanding of how best to assess mental disorders and provide mental health services in general health care settings. Methods and tools to study this area at the patient, provider and organizational level are needed.
8. Clinical epidemiology research. This program includes epidemiologic studies of mental disorders in clinical settings, including studies dealing with clinical decision-making in personal-encounter care for individual patients; studies concerned with the procedures and standards needed for scientifically rigorous studies of complex clinical phenomena that occur in patients; pharmacoepidemiology studies; research to identify risk factors for the development of mental disorders in clinical settings; factors important in the natural history of mental disorders, including co-morbid conditions, and the rates of occurrence of mental disorders in clinical populations. Methods to study decision-making, to more efficiently and accurately assess disorders and levels of functioning, and to study the interaction of patients and clinicians in various settings are needed.
9. Diagnosis and disability assessment research. This program includes research that develops and evaluates standardized methods for measuring and classifying psychiatric disorders and their disablements; studies the validity and boundaries of diagnostic

categories and disablement assessments; develops computer software relevant to the diagnosis, classification, and study of psychiatric disorders and their disablements; studies of the frequency of psychiatric disorders and their associated disablements in clinical settings, and in general and special community groups. Methods to reliably and accurately assess psychiatric disorder and disability in clinical settings are needed.

- B. *Adult and Geriatric Treatment and Preventive Interventions Research.* The focus is on the treatment, prevention, and rehabilitation of mental disorders in adults, including older persons. The focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, the variety of community and institutional settings in which treatment is provided, and the range of outcomes measured. Disorders studied include: all mental disorders; Alzheimer's disease and related dementias; suicide; eating disorders, sleep disorders; and disorders related to the menstrual cycle. Interventions studied include pharmacologic approaches (individual drugs and combinations of drugs), somatic approaches (e.g., electroconvulsive therapy), behavioral and psychotherapeutic approaches (e.g., cognitive therapy). Research is supported on individual and combined approaches; time frame includes acute, continuation, and maintenance studies and long-term symptomatic management and improvement of functional status.

Human subjects include adult and geriatric age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders (e.g., anxiety + depression), substance abuse (e.g., depression + alcohol abuse), brain disease (e.g., stroke + depression), or physical illnesses (e.g., sensory impairment + psychosis). Normal controls are often used in studies. Settings of research include academic or non-academic specialty services (psychiatry, neurology, etc.), primary care settings, hospitals, nursing homes, outpatient clinics, and home health under managed care or fee-for-service. Other settings for research include

occupational health programs, community centers, and correctional facilities. Research must include active interventions for mental disorders and behavioral dysfunctions; observational studies are assigned elsewhere. Areas supported are: trials to establish the short- and long-term efficacy of interventions; studies that assess the effectiveness/cost effectiveness of interventions in standard or usual practice settings; off-label or innovative applications of established treatments; comparative studies of alternative treatments; clinical pharmacokinetic/pharmacodynamic studies; strategies for augmentation/combination and for reduction/taper; correlates of treatment response/basis for treatment failure with established agents; studies designed to develop and refine methodology for use in intervention research; and treatment algorithms/strategies for improvement of clinical care.

1. Somatic Treatments Program. Areas include electroconvulsive therapy (ECT), repeated transcranial magnetic stimulation (RTMS), bright light, physical exercise, and similar approaches in all areas of Branch program support.
2. Adult Psychopharmacology and Geriatric Psychopharmacology Programs. Areas include clinical psychopharmacology (Phase 3 and 4 type studies), new/innovative applications for established treatments, studies of side effects and adverse reactions to pharmacologic treatment (tardive dyskinesia, cognitive impairment etc.), new approaches to dosing (e.g., in geriatric patients), treatment duration and intensity, and tapering/cessation/withdrawal strategies in all areas of program support.
3. Adult Psychotherapy and Geriatric Psychotherapy Programs. Application of new psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and innovative applications of new treatments in all areas of program support.

4. Combined Treatments Program. All research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention). Multiple approaches within the same class of modalities (e.g., two drugs or two psychotherapies) would not be considered combined treatment for programmatic purposes.
  5. Preventive Interventions Program. Preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence, inappropriate resource use) or side effects (prevention/minimization of tardive dyskinesia, etc.). A specially designated programmatic focus is in the area of suicide prevention.
  6. Rehabilitative Interventions. Rehabilitative interventions related to optimizing long-term outcomes of treatment with respect to function, disability, and quality of life.
- C. *Child and Adolescent Treatment and Preventive Intervention Research.* The branch supports research focusing on the treatment, prevention, and rehabilitation of mental disorders in children and adolescents. The focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, the variety of community and institutional settings in which treatment is provided and the range of outcomes measured. Disorders studied include all mental and behavioral disorders. Interventions studied include pharmacologic approaches (individual and combination medications), somatic approaches, behavioral and psychotherapeutic approaches. Research is supported on individual and combined approaches, time-frame includes acute, continuation, and maintenance studies and long-term symptomatic management and improvement of functional status.
- Human subjects include child and adolescent age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders and behavioral problems (e.g., anxiety and depression), substance abuse (e.g., depression and alcohol abuse), brain disease or physical illnesses. Normal controls are often used in studies. Settings of research include academic or non-academic services (child psychiatry, neurology, etc.), primary care settings (e.g, pediatrics), hospitals, group homes, foster care, schools, and outpatient clinics under managed care or fee-for-service. Other settings include community centers, group homes and juvenile justice facilities. Research must include active interventions for mental disorders and behavioral dysfunctions; observational studies are assigned elsewhere. Areas supported are: trials to establish the short- and long-term efficacy of interventions; studies that assess the effectiveness/cost effectiveness of interventions in standard or usual practice settings; off-label or innovative applications of established interventions; comparative studies of alternative interventions; clinical pharmacokinetic/pharmacodynamic studies; strategies for augmentation/combination and for reduction/taper; correlates of treatment response/basis for treatment failure with established agents; treatment algorithms/strategies for improvement of clinical care; and studies designed to develop and refine methodology for use in intervention research.
1. Pharmacologic Treatment Intervention Program. Areas include clinical psychopharmacology (Phase 3 and 4 type studies), new/innovative applications for established treatments, studies of side effects and adverse reactions to pharmacologic treatment (e.g., tardive dyskinesia, etc.), tapering/cessation/withdrawal strategies and somatic treatments in all areas of program support.
  2. Combined Intervention Program. Areas include all research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention). Multiple approaches within the same class of modalities (e.g., two medications or two psychotherapies) would not be

considered combined treatment for programmatic purposes.

3. Psychosocial Intervention Program. Areas include development and application of new psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and innovative applications of new treatments in all areas of program support.
4. Preventive Intervention Program. Areas include all preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence, inappropriate resource use) or side effects (prevention/ minimization of tardive dyskinesia, etc.). A specially designated programmatic focus is in the area of suicide prevention.

For further information on services and intervention research, contact:

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#### **Other Research Topic(s) Within Mission of Institute**

For general questions about the mission of NIMH, prospective applicants are encouraged to contact:

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#### **NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)**

The mission of NINDS is to reduce the burden of neurological disease—a burden borne by every age group, by every segment of society, by people all over the world. To this end, the Institute supports and conducts research on the healthy and diseased brain, spinal cord, and peripheral nerves. Hundreds of disorders afflict the nervous system. Common killers and disablers such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke, epilepsy, and autism are well known. Other disorders we study may be known only to the patients and families affected, their doctors, and scientists who look to rare disorders for help in understanding the brain as well as treating more common diseases.

Examples of research topics within the mission of the NINDS that may be of interest to small businesses are shown below. For additional information about areas of interest to the NINDS, please visit our home page at <http://www.ninds.nih.gov>.

Extramural research is organized in the following programmatic areas within NINDS: neurodevelopment, neurogenetics, repair and plasticity, synapses and circuits, systems and cognitive neuroscience, neurodegeneration, neural environment, and technology development. Specific areas of interest are listed below:

#### **Neurodevelopment**

- A. Development of computer software to permit reconstruction of magnetic resonance imaging (MRI) from unrestrained patients or animals that may change position within the MRI magnetic field.

- B. Development of technology to assess fetal neurological integrity such as fetal MEG.
- C. Non-invasive monitoring of brain function such as improvements in PET imaging, MRI imaging and spectroscopy, and methods of optical imaging such as development of near infrared spectroscopy (NIRS) for monitoring of changes in cerebral oxygen saturation, cerebral blood flow and volume, and oxygen utilization in the brain, and for functional imaging utilizing scattering and absorption characteristics of brain tissue.
- D. Non-invasive techniques for structural imaging, such as near infrared imaging.
- E. Development of computerized histological tomographic brain atlas graphics, which can be stored and manipulated on a personal computer for teaching, research data modeling and display, and correlation with clinical neuroimaging.
- F. Development of practical imaging modalities in extremely ill very low birth weight infants.
- G. Non-invasive techniques for assessment and continuous bedside monitoring of cerebral function in the neonate, such as, but not limited to, functional near infrared spectroscopy and amplitude-integrated EEG.
- H. Development of improved technology for MRI imaging of infants and small children, for example, specially designed pediatric sized head coils, or devices to minimize movement artifact in unsedated infants.

### **Neurogenetics**

- A. Development of central nervous system cell lineages for treatment of neurodevelopmental and degenerative disorders.
- B. Development of embryonic stem cell models of nervous system development and function.
- C. Development of technology for the production of high quality cDNA libraries from small tissue samples of the brain during development and in response to disease, injury or pharmacological agents.
- D. Identification of optimal DNA vector systems to standardize and expedite the

sequencing of cDNA libraries derived from microdissected brain tissues.

- E. Development of technology for microdissection of brain tissue for single cell analysis of gene expression.
- F. Development of informatics systems to expedite the analysis and use of sequence data that will be derived from projects to identify novel genes and to map temporal and spatial dimensions of gene expression in the brain.

### **Repair and Plasticity**

- A. Neural Prostheses and Deep Brain Stimulation
  1. Design, development, and evaluation of neural recording and stimulating microelectrodes for neural prostheses and deep brain stimulation.
  2. Development of thin, insulating coatings to make implanted electronic packages impervious to the corrosive action of body fluids and tissues.
  3. Development of transducers of position, touch, and force for use in functional electrical stimulation systems.
  4. Development of electrodes for sensing specific neurotransmitters.
  5. Non-invasive methods of focally stimulating small populations of neurons within the body.
  6. Development of communication aids for individuals with "locked-in syndrome."
  7. Development of a complete system utilizing existing microelectrodes, lead wires and percutaneous connectors to transfer neural signals outside the body.
  8. Develop new high charge density electrode materials.
  9. Development of a method to repeatedly inhibit neuronal electrical activity in a safe and effective manner.
  10. Development of a non-invasive method of selectively stimulating and/or inhibiting small groups of nerve fibers within a nerve trunk.

11. Development of materials to minimize scarring following surgery in the central nervous system.
  12. Development of techniques for precise functional placement of microelectrodes within the central nervous system.
  13. Neural control of micturition and defecation for individuals with spinal cord lesions.
- B. CNS Trauma and Rehabilitation
1. Development, testing, and evaluation of devices, methods, or drugs to aid the neurologically injured.
  2. Means of assisting or achieving restitution of function in victims of injury to the nervous system.
  3. Develop transgenic, knockout and inducible knockout animal models for stroke and CNS trauma research.
  4. Develop technology for data gathering and analysis for assessment of multiple parameters of ICU recording in brain trauma.
  5. Develop reporting instruments for data collection and analysis in clinical studies of head injury.
  6. Develop a novel means of preclinical testing for new and promising therapies for acute and chronic central nervous system injury.
  7. Development of a simplified registry and follow-up technique for patients with brain and spinal cord injury.
  8. Development of monitors for such modalities as intracranial pressure, brain temperature, and cerebral blood flow.
  9. Development of consortia to share data on head injury patients, design clinical protocols, and conduct clinical trials in traumatic brain injury.
  10. Establishment of networks to test pharmaceutical agents in animal models of CNS trauma.
- C. Neuroimaging
1. Development of ultrasound imaging methods for the central nervous system.
  2. Development of functional imaging techniques.
  3. Development of imaging techniques to track the course of injury and repair following spinal cord injury.
- D. Stem Cell Biology
1. Development of a website and database for posting and discussion of protocols used in harvesting, maintaining in culture, and inducing differentiation of neural stem cells.
  2. Development of a stem cell repository for the storage of embryonic stem cells and immortalized cell lines, and for making these reagents readily available to the research community.
  3. Develop efficient and reproducible methods for harvesting and storing stem cells for research use.
  4. Develop methods for the delivery of growth factors, cells, genes and other agents to specific sites within the nervous system.
  5. Develop markers for the identification and/or harvesting of stem and progenitor cells in the nervous system and in non-neural tissues.
  6. Develop methods for phenotyping stem and progenitor cells in the nervous system.
  7. Use of mutant and transgenic mice or rats to study the effect of identified genetic alterations on neurogenesis in the adult central nervous system.
- E. Axonal guidance and synapse formation
1. Develop biomaterials to serve as paths for axonal guidance across a site of injury.
  2. Develop biomaterials to promote sprouting and directed growth of axons toward specific sites in the central nervous system.
  3. Develop biomaterials to promote dendritic growth and stability, and synapse formation in localized areas.

## **Systems and Cognitive Neuroscience/Channels, Synapses and Circuits**

### **A. Epilepsy**

1. Devices for automated detection and quantification of seizures.
2. New therapies both for the control of seizures and for the prevention of the development of epilepsy.
3. New formulations and delivery systems for antiepileptic drugs.
4. New models of seizures and epilepsy useful for screening therapies.
5. Improved methods of monitoring compliance/medication dispensing.

### **B. Sleep Neuroscience**

1. New therapies for sleep disorders.
2. New methods for quantifying optimal alertness.
3. Models of neurological sleep disorders.
4. Novel applications of evoked potentials to sleep neuroscience.
5. Further development of portable devices that facilitate cost-effective screening for potential sleep disorders, and can be used to monitor the progress of already diagnosed sleep disorders.

### **C. Pain**

1. Development of objective methods for quantitative assessment of pain, including development of a quantitative sensory testing battery for pain patients.
2. Development of novel pain model systems, particularly more accurate pre-clinical experimental models.
3. Development of tools to elucidate potential analgesic targets, and models for testing and validating these for efficacy in patients.
4. Development of new diagnostic tools for different pain mechanisms and objective measures of analgesic drug action.

### **D. Neuroimaging**

1. Development of devices for artifact-free monitoring of vital neurological parameters during MRI procedures involving very high static and dynamic magnetic fields (greater than 2 Tesla) and high-energy microwave radiation typical of the MRI environment.
2. Development of functional imaging techniques.
3. Development of combined imaging strategies, i.e. fMRI and PET.

## **Neurodegeneration**

### **A. Neurological Disorders**

1. Testing of candidate drugs for treatment of specific diseases according to a prescribed protocol and involving limited numbers of animals.
2. Development and preliminary testing of instruments, devices, or drugs that enhance diagnostic, treatment, or monitoring capabilities.
3. Identification or development of animal models for research on degenerative disorders.
4. Development of early or presymptomatic diagnostic procedures for degenerative disorders.
5. Epidemiology of nervous system diseases/disorders.
6. Development of an ambulatory monitor to measure fluctuations of movements in patients with degenerative neurological disorders.
7. New delivery methods of medications for degenerative neurological disorders.
8. Development of immortalized cell lines with neuronal phenotype, particularly spinal motor neurons, for in vitro modeling of amyotrophic lateral sclerosis.
9. Development of experimental animal models of ALS.
10. Development of drugs to treat ALS.

## **Neural Environment**

### **A. Infectious and Immune Disorders**

1. Development of therapies to prevent or arrest auto-immune neurological disorders, e.g., multiple sclerosis.
  2. Development and studies of drugs with high blood brain barrier permeability intended for treatment of CNS infections including HIV related opportunistic infections.
- B. Stroke**
1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of stroke patients.
  2. Mass spectrometry for the analysis of protein expression in the ischemic CNS.
  3. Transgenic, knockout and inducible knockout animal resources for stroke research.
  4. Brain specific gene and protein transfer methods for delivery to cerebral vessels, neurons, or glia in the ischemic CNS.
  5. Methods and devices for high throughput genomic and proteomic expression and data analysis in stroke.
  6. Methods to transiently suppress gene and protein expression in brain ischemia.
  7. Synthesis of radiolabeled ligands or similar substances for highly specific receptor sites that would aid in the identification of varying degrees of ischemia to brain cells.
  8. Refinement of functional, structural and metabolic imaging techniques for stroke.
  9. Surrogate markers for neurodegenerative, vascular, and immune diseases of the brain.
- C. Brain Tumors**
1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of CNS tumors.
  2. Advancement of molecular analysis of DNA, RNA and protein in CNS tumors.
  3. Surrogate markers for cerebrovascular, immune, and infectious diseases and CNS tumors.
  4. Develop methods for identification of specific neural cell lineages.
  5. Techniques for brain specific antisense, gene and protein transfer into cerebrovascular, neurons, or glial cells in brain tumors.
  6. Methods to deliver brain specific proteins and genes through the blood-brain and blood-CSF barriers for targeting CNS tumors.
  7. Mass spectrometry for the analysis of protein in the CNS and in brain tumors.
  8. Highly specific radiolabeled markers for different types of brain tumors that can be used under histopathological or brain imaging conditions.
  9. Development of an intracranial pressure monitor.
  10. Refinement of functional, structural and metabolic imaging techniques for brain tumors.
  11. Methods and devices for high throughput genomic and proteomic expression and data analysis in brain tumor.
- Technology Development**
- A. Animal models, including genetic and experimental models of neurological disorders; examples include mouse mutants, models of spinal cord injury or traumatic brain injury, epilepsy, and channelopathies.
  - B. Neuroinformatics, including relational software for genetic, functional, and anatomical data; databases; and websites for data sharing.
  - C. Computational tools for understanding both cellular and systems level function in the nervous system.
  - D. Approaches to recording and stimulating neural activity, including single cells, cellular ensembles, and brain regions or fiber tracts.
  - E. Imaging tools, including MRI, fMRI, MRS, PET, MEG, optical and infrared, and

ultrasound, both for human and animal studies.

- F. Approaches to identify and characterize genes involved in function and pathology in the nervous system, including microarrays, genetic linkage methods, mutagenesis, expression analysis, and in situ localization.
- G. Approaches to identify and characterize proteins involved in function and pathology in the nervous system, including electrophoretic, immunochemical, and mass spectrometric analyses.
- H. Therapeutic drug discovery, including the development of molecular, cellular, or animal-behavioral screening assays; high-throughput screening approaches; and preparation of drug candidate chemicals or chemical libraries by traditional or combinatorial chemical approaches.
- I. Bioengineering, including neural prostheses.

#### **Other Research Topics Within Missions of Institute**

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#### **NATIONAL INSTITUTE OF NURSING RESEARCH (NINR)**

The NINR supports research focused on biological and behavioral aspects of critical

health problems that confront the Nation. Emphasis is on seeking ways to reduce the burden of illness and disability by understanding and easing the effects of acute and chronic illness, improving health-related quality of life by preventing or delaying the onset of disease or slowing its progression, establishing better approaches to promote health and prevent disease, and improving clinical environments by testing interventions that influence patient health outcomes and reduce costs and demand for care.

For additional information about areas of interest to the NINR, please visit our home page at <http://www.nih.gov/ninr/>.

#### **Research and Development of Technologies that Promote Alleviation, Adaptation, or Management of Symptoms**

- A. Technologies to be used in the hospital, long-term care or home setting to validate clinicians/patients' assessment of chronic problems such as congestive heart failure, cystic fibrosis, organ failure, dementia, renal disease, and asthma.
- B. Devices to improve delivery of nursing care for patients who have restricted or impaired movement, such as spinal cord injury, cystic fibrosis, intraocular trauma, major burns, tethered to instrumentation ECMO, ventilators, IABP, or orthopedic fixation devices.
- C. Devices to assist teenagers to quit smoking.

#### **Research and Development of Technologies to Enhance Self Care and Clinical Care**

- A. Technologies to assist patients to adhere to chronic regimens such as reminding children to take steroid inhalers during the day for asthma; alerting obese adults when high calorie and fat content foods are about to be eaten; and prompting sedentary adults to exercise.
- B. Telehealth technologies to improve delivery of patient care such as assessing injury severity or traumatic injury in children and adults and transmitting this information to acute care settings for assessment and evaluation; and communicating signs and symptoms of clients at home to health care providers in distant locations; and tailoring

nursing care for diverse patients in a wide variety of settings.

- C. Technologies to treat chronic wounds that fail to heal, specifically decubitus ulcers, venous stasis ulcers, and diabetic ulcers.
- D. Technologies to be used in the hospital or home care setting to monitor or assess preterm infants.

#### **Other Research Topic(s) Within the Mission of Institute**

For additional information on research topics, contact:

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#### **NATIONAL CENTER FOR RESEARCH RESOURCES (NCRR)**

The NCRR develops and supports critical research technologies and shared resources that underpin research to maintain and improve the health of our Nation's citizens.

For additional information about areas of interest to the NCRR, please visit our home page at <http://www.ncrr.nih.gov>.

#### **Research and Development in Instrumentation and Specialized Technologies for Biomedical Research**

- A. New or improved instruments, devices, and related methodologies to facilitate biomedical or behavioral research. Instrumentation includes but is not limited to mass spectrometry, nuclear magnetic resonance, electron spin resonance, fluorescent or kinetic or laser spectroscopies, X-ray absorption/

diffraction, electron or confocal or atomic force microscopies, and flow cytometry.

- B. Development of computer science/technology to study biomedical or behavioral research problems, e.g., computer visualization (graphics and virtual reality/environments), image processing, computer modeling/simulation including neural networks, structure-based drug design; development of new bioinformatics technology infrastructure.
- C. Biomedical engineering approaches for basic/clinical research that have potential for preventing or treating disease and/or significantly reducing health care costs, e.g., biomaterials, microsensors, monitoring devices, non-invasive diagnostic approaches, alternatives to radioactive-based methods, robotics, and drug delivery systems.

Electron Microscopy, X-ray Diffraction, Other Topics

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Imaging, EPR

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NMR, Optical Microscopy, Laser Applications

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Mass Spectrometry

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**Research and Development in Comparative Medicine**

- A. Development of improved reagents and cost-effective methods to accurately screen and diagnose selected laboratory animal

diseases, and for performing overall assessments of animal quality and health status. An urgent need currently exists for the development of improved methods for the detection of active tuberculosis in nonhuman primates.

- B. Development of vaccines and new therapeutic agents for the prevention and/or control of selected laboratory animal diseases. One high priority need is for the development of a vaccine to prevent Herpes B virus in nonhuman primates.
- C. Development of commercially valuable reagents from lower organisms or established cell cultures.
- D. Development of cost-effective methods for culture and/ or preservation of commercially valuable organisms, including specific types of bacteria and other microorganisms.
- E. Development of cost-effective husbandry and colony management techniques, equipment, and/or new approaches to improve laboratory animal welfare and assure efficient and appropriate research use.
- F. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control.
- G. Identification, development and characterization of spontaneous vertebrate animal models for studies on various types of human disease.
- H. Development and refinement of new technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.
- I. Development of new and/or improved methods for producing transgenic animals and their applications for gene therapy research on special categories of human diseases.
- J. Development of improved reproductive biology techniques (e.g., cloning techniques; embryo splitting) to produce genetically identical laboratory animals.
- K. Development of technologies for the extracorporeal fertilization of eggs (in vitro fertilization, fertilization by sperm injection, xenogenous, or intraspecific fertilization,

etc.) to allow production of new animal models for human diseases.

- L. Development of technologies for improved embryo transfer within a single animal species or of intraspecific embryo transfer to allow preservation of rare, unique, or endangered animal species that may have unique value as animal models for human disease.

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### **Clinical Technology Applications**

- A. Development of patient-oriented research technologies. This includes therapies, diagnostics, sensors, and imaging technologies used for patient diagnosis, monitoring, and treatment.
- B. Diversification of methods used for clinical studies of disease states, such as micro-analytical sensors or imaging devices.
- C. Miniaturization of existing biomedical technologies for adaptation to pediatric use.
- D. Development of artificial tissues and organs for medical use.
- E. Development of vehicles for drug delivery, including for patient groups with a potential for altered pharmacology or compliance, such as children or the elderly.
- F. Development of bioinformatics technology: (1) collection, collation, and archiving of databases; (2) assuring compatibility with other databases; (3) protected storage and transmission of confidential medical data; and (4) software which facilitates the review or implementation of clinical trial protocols; (5) software and hardware applicable to tying in data from multiple and simultaneous clinical protocols across multiple clinical sites; and (6) methods and instrumentation to support clinical imaging data.
- G. Development of vectors for gene therapy, with improved means of: (1) targeting specific cells and/or tissues; (2) transduction and expression; (3) delivery to patients; and/or (4) production and purification.

- H. Development of DNA microarray chip technology for studies of human diseases and methods and techniques for the analyses, storage, and interpretation of accumulated data.

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### **Development of Discovery-Oriented Software for Science Education**

Development of new discovery-oriented educational software on health science topics that targets K through 12 students is sought. Topics can range from basic cell biology to human diseases. Development of this software may be directed toward the adaption of existing or recently developed educational programs for interactive learning. A broad dissemination is strongly encouraged. This effort is intended to yield efficient and user-friendly educational units for K through 12 students, and which can be extended to enhance the health science literacy of the general public.

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## **NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)**

"The general purposes of the National Center for Complementary and Alternative Medicine (NCCAM) are the conduct and support of basic and applied research, research training, and other programs with respect to identifying, investigating, and validating complementary and alternative treatment, diagnostic, and prevention modalities, disciplines and systems" (P.L. 105-277). To meet this mandate, NCCAM supports research and training programs that increase our knowledge of, and improve research methods on, complementary and alternative medicine.

For additional information about areas of interest to the NCCAM, please visit our home page at <http://nccam.nih.gov>.

### **Education and Public Information**

- A. Develop innovative teaching and dissemination tools to convey results of complementary and alternative medicine (CAM) research using state-of-the-art technology.
- B. Develop and validate methods for rapid dissemination of CAM-related data to specific target audiences who may play a role in public health actions.
- C. Develop innovative teaching methods for professional and lay-educators to teach the lay-public about CAM; special consideration should be given to appropriate ways to communication with minority and special groups.
- D. Develop user-friendly Internet sites to provide scientific and practice information about CAM.
- E. Develop and test innovative education approaches, including CD ROM technology and the Internet, that can be used in training health care professionals and paraprofessionals in CAM.
- F. Develop and test innovative education approaches, including CD ROM technology and the Internet, for improving the knowledge of CAM among the general public, including school age children, minorities and special groups.

### **Patient Management**

- A. Develop and validate tools to aid in the clinical management of patients, including selection of appropriate CAM interventions, process evaluation, assessment of outcome, aftercare, and patient tracking, in various treatment settings.
- B. Develop and validate assays that identify patients who will benefit most from specific CAM interventions (i.e., identify responders from non-responders).
- C. Develop and validate methods to collection clinical data in a practice-based setting.
- D. Develop and validate methods to credential CAM providers in a uniform fashion.
- E. Develop and test technologies to assist patients in adherence to chronic CAM regimens, such as diet-based or mind-body interventions.

### **Botanical Products**

- A. Develop and validate methods to test the clinical applications of natural products both in vivo and in vitro.
- B. Develop methods for the cultivation and extraction of standardized natural product that meet the GMP requirements of the FDA IND process.
- C. Develop simple biological assays that can be used to monitor the levels of natural products of interest in simple whole extracts.
- D. Develop and validate methods for chemical and biological identification of active ingredients in botanicals.

### **Research-related issues**

- A. Develop innovative ways using state-of-the-art-technology to reanalyze existing data sets containing information on CAM, including those from the Centers for Disease Control or Health Care Financing Administration.
- B. Develop methods to validate the clinical usefulness (validity, reliability, responsiveness and utility) and appropriateness of assessment procedures and clinical tests specific to CAM (e.g., physiological measures of chiropractic manipulation, or measures of chi).

- C. Develop innovative, state-of-the-art methods to monitor CAM interventions in a practice-based setting and to correlate these interventions with outcome measure; results should be accessible to other interested parties without compromising the privacy of the individual patient.
- D. Develop and validate methods to compare the Western biomedical diagnostic system with the diagnostic system of other medial systems (e.g., Ayurvedic, traditional Chinese medicine).
- E. Develop and validate animal and in vitro models to study CAM interventions.
- F. Develop methods for the management and analysis of clinical trial data for CAM interventions.
- G. Develop and validate viable sham controls for use in clinical trials of CAM interventions.
- H. Develop and test new technologies and instrumentation for the objective study of CAM products and practices.
- I. Develop and test new technologies, basic models and instruments for the study of CAM diagnostic and therapeutic systems.

#### **Other Research Topic(s) Within Mission of the Center**

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#### **NATIONAL LIBRARY OF MEDICINE (NLM)**

The NLM supports research on the organization, management, and utilization of health knowledge and information. Volume and demand for health science knowledge overwhelm traditional methods of information access for health professionals. Clinician, investigator, and student find it increasingly difficult to integrate vast bodies of data. Innovative methods, systems, and services for managing information that incorporate speed, responsiveness, and economy are needed. State-of the-art computer and communication technologies offer opportunities for the creative development of such information access mechanisms for health professionals, their students, and their patients.

For additional information about areas of interest to the NLM, please visit our home page at <http://www.nlm.nih.gov>.

#### **Molecular Biology**

The appearance of new experimental methods has greatly increased the volume of molecular data for all the basic medical sciences, including the neurosciences. To help integrate such data NLM is interested in:

- A. Software algorithms and database query methods capable of translating natural language questions into appropriate retrievals from multiple related factual databases.
- B. Software for data management and analysis for genetic linkage mapping, physical mapping, and DNA sequences.
- C. Expert system techniques for automatic generation of annotation information and creation of linkages among related databases via explicit pointers or common vocabulary.
- D. Algorithms capable of predicting structure and/or function in model biological systems.

#### **Medical Informatics**

There are broad needs for innovative computer software and systems to assist changing dimensions of health care by developing knowledge bases, information synthesizing mechanisms, decision support systems, and similar modalities:

- A. Mechanisms to integrate new information into existing knowledge bases, and software to extract and analyze information from large patient record databases (i.e., secondary data aggregation).
- B. Development of organizing and synthesizing systems that closely match specific health problem areas to help health care providers manage information better.
- C. Systems, devices, or programs that facilitate utilization of electronic medical record systems in clinical practice, for such functions as chart entry, ordering, and scheduling.
- D. Innovative, interactive multimedia programs for health professions education, such as information sources for learners and tools to support educational program administration.
- E. Systems that facilitate network migration to bring the fullest possible range of learning materials to educator and learner.
- F. Better search engines that filter, organize, and index.

#### **Other Research Topic(s) Within Mission of NLM**

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#### **TRANS-NIH RESEARCH PROGRAMS**

##### **Development of Synthetic and Natural Biomaterial Reference Materials**

The NIH invites applications for the development of synthetic or natural biomaterial reference materials (RMs). RMs are used for standardization of studies of interactions

between materials and blood and tissues, for calibration of physicochemical test methods, and/or for reference controls in physical, chemical, and materials structure characterization tests. All innovative developments of biomaterials and devices also need measurements to demonstrate their innovation and improvement. Because RMs lie at the heart of measurement technology, funding for their development could play a key role in future advances in biomaterials and biomedical material device technologies.

Industry uses biomaterial RMs for quality assurance and traceability. The Food and Drug Administration considers them useful for comparing new biomaterials, or new uses of biomaterials, with existing standards and materials. In order to have maximum utilitarian value, it is intended that these biomaterial RMs be stored at, and distributed by, the National Institute of Standards and Technology (NIST). Hence, they must be produced to meet the stringent requirements of the NIST Standard Reference Material Program. *It is important for applicants to contact NIST (Dr. John A. Tesk, (301) 975-6799; Email: [john.tesk@nist.gov](mailto:john.tesk@nist.gov)) to obtain detailed information on requirements of that program prior to preparing and submitting their applications.*

Biomaterial RMs may be synthetic polymers, ceramics, metals, or mixtures of these, or may be derived from living tissues. The choice of RM to be developed is up to the applicant but must be fully justified based on the applicant's knowledge of the magnitude of the current or potential utilization of the biomaterial. RMs of known particular value include: (1) silica-filled poly(dimethylsiloxane), (2) aliphatic polyether urethane, (3) poly (vinylchloride), (4) poly(methylmethacrylate), (5) expanded poly (tetrafluoroethylene) of varying standardized internodal distances, (6) oxygen permeability standards, and (7) carbon materials used in mechanical heart valve designs.

RMs must be of appropriate size and shape. The form in which the reference material is produced and the tests necessary to characterize the material are the decision of the applicant based on the end use of the material. The applicant may consider NIST as a potential subcontractor for measurement and other professional services.

For additional information on this topic, please contact:

Dr. Christine A. Kelley  
Bioengineering Research Group  
National Heart, Lung, and Blood Institute  
6701 Rockledge Drive, Room 9180  
Bethesda, MD 20892-7940  
(301) 435-0513; Fax: (301) 480-1336  
Email: [ck53r@nih.gov](mailto:ck53r@nih.gov)

### National Center on Sleep Disorders Research

The National Center on Sleep Disorders Research (NCSDR) was established within the National Heart, Lung, and Blood Institute (NHLBI) as a result of the National Institutes of Health (NIH) Revitalization Act of 1993. Its mandate is to conduct and support research, training, health information dissemination, and other activities with respect to sleep disorders, including biological and circadian rhythm research, basic understanding of sleep, chronobiological and other sleep related research and to coordinate the activities of the Center with similar activities of other Federal agencies, including the other agencies of the National Institutes of Health, and similar activities of other public entities and nonprofit entities.

Three specific types of research are emphasized: basic research, using state-of-the-art approaches, to elucidate the functions of sleep and the fundamental molecular and cellular processes underlying sleep; patient-oriented research to understand the cause, evaluate the scope, and improve the diagnosis and treatment of sleep disorders; and applied research to evaluate the scope and consequences of sleepiness and to develop new approaches to prevent impaired performance during waking hours.

Research opportunities of interest to small businesses may include, but are not limited to, development of:

- A. Advanced, inhome assessment of sleep disturbances and therapeutic effectiveness.
- B. Countermeasures for specific causes of sleepiness, including methods to alter the output of the circadian clock to optimize sleep and wakefulness.
- C. Development of new technologies and instrumentation scaled for high-throughput

phenotypic characterization of sleep parameters in mice.

- D. Efficient, objective measures of daytime sleepiness.
- E. Health education methodologies for patients, families, or communities to prevent or cope with sleep disorders or to reduce their impact.
- F. High volume, inexpensive assays for monitoring gene expression in model systems.
- G. Improved methods to diagnose respiratory disorders of sleep in infants, children, and adults.
- H. Interventions to prevent and manage sleepiness to improve productivity and safety.
- I. Methods and techniques to monitor tissue oxygenation.
- J. Methods that will improve patient compliance with treatments for respiratory disorders of sleep.
- K. New therapies for sleep disorders and pharmacological agents to increase alertness.
- L. Noninvasive imaging technologies for evaluating the neurophysiology, regional brain blood flow, and neural pathway changes accompanying sleep and wakefulness.
- M. Novel pharmacological approaches for the treatment of sleep apnea.
- N. Physiological, biochemical, and behavioral assays of sleepiness and methods to monitor levels of alertness continuously and over extended periods of time.
- O. Portable, ambulatory, cost-effective instruments to screen and diagnose sleep disorders.

For additional information on research topics, please contact:

Dr. Michael Twery  
Acting Director, National Center on Sleep Disorders Research  
National Heart, Lung, and Blood Institute, NIH  
6701 Rockledge Drive, Room 10038  
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## **CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)**

The CDC serves as the national focus for developing and applying disease prevention and control, environmental health and health promotion and health education activities designed to improve the health of the people of the United States. To accomplish its mission, CDC identifies and defines preventable health problems and maintains active surveillance of diseases through epidemiologic and laboratory investigations and data collection, analysis, and distribution; serves as the PHS lead agency in developing and implementing operational research aimed at developing and testing effective disease prevention, control and health promotion programs; administers a national program to develop recommended occupational safety and health standards and to conduct research, training, and technical assistance to assure safe and healthful working conditions for every working person; develops and implements a program to sustain a strong national workforce in disease prevention and control; conducts a national program for improving the performance of clinical laboratories; and develops programs to prevent premature death and avoidable illness and disability caused by noninfectious, non-occupational environmental and related factors.

CDC is responsible for controlling the induction and spread of infectious diseases, and provides consultation and assistance to other nations and international agencies to assist in improving their disease prevention and control, environmental health, and health promotion activities.

For additional information about areas of interest to the CDC, please visit our home page at <http://www.cdc.gov>.

## **NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)**

<b>NIOSH will accept SBIR grant applications ONLY on the August 1 and December 1, 2001 receipt dates.</b>
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The NIOSH plans, directs and coordinates the national program effort to develop and establish recommended occupational safety and health standards and to conduct research, training, and related activities to assure safe and healthful working conditions for every working man and woman. NIOSH has both a regular grant

program and an SBIR grant program; the purpose of both is to develop knowledge that can be used in preventing occupational diseases and injuries. In the regular NIOSH grant program, the following types of applied research projects are supported: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational diseases and injuries; methods research to develop more sensitive means of evaluating hazards at work sites, as well as methods for measuring early markers of adverse health effects and injuries; control research to develop new protective equipment, engineering control technology, and work practices to reduce the risks of occupational hazards; and demonstrations to evaluate the technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system. The SBIR grant program is focused on the following topics:

### **Control Technology and Personal Protective Equipment**

Engineering controls, administrative policies, and personal protective equipment are needed to manage exposures to occupational hazards. Engineering controls include substitution of a safe material for a hazardous one, design changes to equipment, or modification of work methods to eliminate or reduce hazards. Changes in work practices and management policies and training programs are examples of administrative controls. In some cases where it is not otherwise possible to maintain a healthy work environment, personal protective equipment such as respirators and protective clothing can be used to isolate workers from the hazard. Research is needed to develop and evaluate control strategies for specific hazards and to assure their practicality and usability in workplaces.

- A. Investigate the effectiveness of existing or proposed engineering controls (including retrofit solutions).
- B. Develop control measures for new workplace hazards.
- C. Identify the specific hazardous parts of a job that contribute most to the actual exposure, including personal hygiene where contamination of surfaces, clothing, or skin may occur.

- D. Evaluate the practical utility in the workplace of proposed personal protective equipment, when it is the only available control option.
- E. Design personal protective equipment that will fit the anthropometric diversity in today's workforce.
- F. Develop alternatives to pesticide application and hazardous waste remediation.
- G. Develop micro sensing devices to notify workers before chemicals break through protective clothing and identify failures in containment systems for hazardous materials.
- H. Create and test new materials for clothing to protect against chemical and physical hazards.
- I. Develop information dissemination methods to help businesses learn about and implement occupational safety and health programs.
- J. Design and evaluate training materials to teach hazards and risks, demonstrate solutions, measure changes in behavior and practices, and improve injury and illness rates.

### **Exposure Assessment Methods**

Exposure assessment is a multi-disciplinary field central to deciding whether and how to use resources for reducing workplace exposures, and to defining exposure-response relationships in epidemiologic studies. Rapid, inexpensive measurement tools and improved data analysis methods are needed for the collection of adequate exposure data and for effective intervention. At least three major gaps in current methods will drive development of exposure assessment methods in the next decade: (1) the lack of sufficiently precise exposure assessments to support accurate epidemiologic studies in the complex environments of today's workplaces, (2) the lack of practical measurement techniques that can be applied at reasonable cost in many workplaces where hazards may exist, and (3) the lack of validated methods for measuring relevant exposure and total dose data directly from biological samples obtained by relatively noninvasive techniques.

- A. Develop computer models to extrapolate information from historical data of limited

exposure measurements to apply to large study populations, and to incorporate short-duration but high-intensity exposures such as leaks or spills into the models.

- B. Develop easy-to-use, direct-reading instruments and test kits to measure exposures rapidly and inexpensively in a variety of workplaces for routine monitoring, evaluating the success of control technologies, and providing data for research studies.
- C. Improve the measurement of low concentrations of chemicals and biomarkers in biological specimens such as blood, urine, saliva and sweat so that such concentrations can be linked to internal dose at the target organs.
- D. Design laboratory analytical methods for inexpensively measuring numerous chemicals in a single sample.
- E. Improve the measurement and interpretation of biomarkers to facilitate evaluation of the effects of structurally similar chemicals.
- F. Formulate exposure survey designs and methods for exposure data analysis to obtain more meaningful data for health risk assessments.
- G. Improve exposure assessment methods so that at-risk workers can be identified, the most cost-effective control and intervention strategies can be determined, better understanding can be gained about exposure-response relationships, and improved baseline data can be collected for standard setting and risk assessment.

### **Intervention Effectiveness Research**

The goal of intervention research is to develop practical strategies and techniques that effectively reduce or prevent workplace injuries and illnesses. Workplace safety and health interventions include but are not limited to developing and implementing specific engineering control technologies, process and work organization changes, information dissemination and health communication practices, worker/management participatory safety and health programs, safety and health training, selective use of personal protective equipment, and inspection and enforcement of protective exposure limits. Intervention research involves the testing and evaluation of

interventions, programs, and policies. Although many intervention strategies have been applied to industrial settings, knowledge about what works best is limited. Corporate safety and health programs, regulatory requirements and voluntary consensus standards, workers' compensation policies and loss-control programs, engineering controls, and educational campaigns are among the types of interventions that need to be developed, implemented, and evaluated.

- A. Develop techniques to evaluate the effectiveness of implemented control technologies.
- B. Determine the barriers to the acceptance of new control technologies and develop approaches to eliminate or alter these barriers, including economic feasibility.
- C. Determine the factors that influence the voluntary adoption of protective work practices.
- D. Evaluate the roles of researchers, consultants, trainers, worker organizations, and industry trade groups as partners in intervention efforts.
- E. Investigate organizational and economic factors that could predict success in prevention programs, and how these programs can be tailored to take account of such factors.
- F. Develop strategies for targeting intervention efforts in the areas of greatest need.
- G. Investigate why managers and workers in some organizations implement occupational safety and health programs when others do not.

### **Surveillance Research Methods**

Surveillance systems describe where occupational hazards, injuries, or illnesses are found, how frequently they are found, whether they are increasing or decreasing, and whether prevention efforts have been effective. The public health community relies on surveillance information to set research and prevention priorities, but critical gaps in current systems limit their usefulness. These systems need to be updated and expanded, and new systems and methodologies need to be developed.

- A. Develop approaches for implementing comprehensive, integrated national

systems utilizing data sources and models of surveillance that exist in the public and private sectors.

- B. Formulate methods to assess nationally or locally the impact of intervention efforts on worker safety and health.
- C. As restructuring of health care delivery systems occurs throughout the United States, develop linkages among the systems to identify, track, and target occupational safety and health problems and provide information for decisions to develop interventions or to improve related medical care.
- D. Investigate hazard surveillance systems as a means of identifying risks and exposures at worksites and industries, including risks associated with prototypes of new technologies, before injuries and illnesses occur.

### **Other Research Topic(s) Within Mission of Institute**

For technical information on research topics contact:

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National Institute for Occupational Safety and Health  
Mail Stop D30  
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Email: [rmf2@niod1.em.cdc.gov](mailto:rmf2@niod1.em.cdc.gov)

For administrative and business management information contact:

Joanne Wojcik  
Centers for Disease Control and Prevention  
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Mail Stop E13  
2920 Brandywine Road  
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## NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

NCIPC will accept SBIR grant applications ONLY on the August 1 and December 1, 2001 receipt dates.

The National Center for Injury Prevention and Control plans, directs, and coordinates a national program to maintain and improve the health of the American people by preventing premature death and disability and reducing human suffering and medical costs caused by non-occupational injury, addressing both intentional injuries that result from violent and abusive behavior and unintentional injuries. The national program encompasses the prevention of non-occupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons. The Center will address injury prevention and control through an orderly sequence of activities beginning with research on causes, circumstances, and risk factors; progressing through research on interventions and their impact on defined populations. These activities then lead to the broad, systematic applications of interventions that are soundly based scientifically.

The CDC is committed to achieving the health promotion and disease prevention objectives of Healthy People 2010, a PHS-led national activity for setting priority areas. Potential applicants may obtain a copy of "Healthy People 2010"; (Full Report: Stock No. 017\_001\_00537\_1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (Telephone (202) 512-1800).

The focus of the research topics should reflect the broad-based need to control injury morbidity, mortality, disability, and costs. These projects may be categorized by the three phases of injury prevention and control. These phases are defined below as prevention, acute care, and rehabilitation. Research topics of interest include, but are not limited to:

### Prevention

There is interest in the development, application, and evaluation of innovative interventions applicable to intentional and unintentional injury. The focus should reflect target populations at high risk for injury and injury consequences,

including minorities, children, the elderly, rural residents, and farm families.

- A. Develop improved smoke alarms (e.g. smoke alarms with a lower frequency alarms for those with high-end hearing loss the most common type; photo-electric smoke alarms powered by lithium 10-year batteries; a smoke alarm that is "always on" because it is hard-wired into a circuit, such as a light circuit with an on-off switch for the light, but the smoke alarm is not turned off).
- B. Develop a practical, valid screening tool to assess an older driver's fitness to drive safely, that takes into account mental, perceptual-motor and physical/medical condition.
- C. Develop devices that help alert drowsy and distracted drivers and prevent inattention that contributes to motor vehicle crashes
- D. Design, develop, and evaluate educational materials to train public health, personnel in injury prevention that could be adapted for medical, nursing and allied health.
- E. Develop and test injury prevention "tool kits" for patient/community use that can be delivered through managed care organizations.
- F. Develop interactive CD-ROMs on safety issues.
- G. Develop cordless phone systems tailored for the elderly and/or disabled (e.g., with large numbers, voice activated and/or pre-programmed 911 and med-alert buttons, etc.) to prevent cord-related falls and improve emergency response.
- H. Design, develop and evaluate a multipurpose helmet for cycling, hockey, skiing, skateboarding, and skating.
- I. Develop and test brief injury intervention modules that could be delivered in medical care and managed care settings to at-risk patients and their families (such as fall prevention, helmet use, alcohol use, supervision, etc.).
- J. Design and develop safety devices for minimizing the likelihood that firearms might be unintentionally discharged, e.g., child proof trigger locks, improved safety latches, indicators for loaded guns and educational materials to keep children and adolescents safe from firearm injury.

- K. Design and develop academic instructional materials on injury prevention and control for grades K through 12 that can be integrated into comprehensive school health education.
- L. Design and develop a school-based curriculum to prevent assaultive behavior among youth based on previously evaluated youth violence prevention programs.
- M. Design and develop educational materials to increase motorcycle safety, such as motorcycle driver training, and safety education.
- N. Design, develop, and evaluate a garment with hip protector that is acceptable, comfortable and effective in preventing a hip fracture in older adult women during a fall.
- O. Develop and test a passive alcohol sensor device to passively measure the blood alcohol level of injured patients arriving at the emergency department.
- P. Design and test a home-based program to assist teens and their parents to manage graduated licensing requirements for new teen drivers.
- Q. Design and develop a safe device to deter dog attacks.
- R. Develop sensors for cars that detect and signal the driver when something or someone (e.g. a small child) is behind the car when it is in reverse.
- S. Design and develop devices and in-vehicle systems that make sitting in the back seat more appealing to children under age 12 (e.g. an activity board with options such as interactive games, music, etc), that is contingent on properly buckling up, and that complies with all federal motor vehicle safety standards.
- T. Develop a low cost retrofit sprinkler system for fire protection that could be added to existing homes and in a variety of ceiling configurations.

### **Acute Care**

The national program encompasses the prevention of non-occupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons.

- A. Development of devices, instruments, methods, models, tests, and computer software related to the full spectrum of acute care of the trauma patient, beginning with the establishment of access to emergency care, response at the injury scene, transportation of the critically injured, to management of postoperative complications such as multiple organ failure syndrome.
- B. There is a need to improve diagnostic modalities in several areas, particularly in those related to perfusion and oxygenation at the tissue level. Further, among those patients whose bleeding have been controlled and will survive the acute phase of injury, the major causes of death are irreversible cerebral damage or uncontrollable cerebral swelling and multiple organ failure. There is an urgent need for research into methods of reducing secondary cerebral injury and of controlling brain swelling and preventing multiple organ failure.
- C. Design, develop and evaluate Emergency Department-based prevention services for the identification and referral of persons at risk for violence or alcohol-related injury.

### **Rehabilitation**

The national program encompasses the prevention of non-occupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons.

- A. Develop adaptive equipment, assistive devices, and instructional materials directed toward preventing or minimizing the secondary complications of individuals with traumatic brain or spinal cord injuries including cognitive learning problems, pressure ulcers, contractures, muscular atrophy, skeletal deformity and other definable conditions.
- B. Design, develop and evaluate educational materials for persons with traumatic brain or traumatic spinal cord injury, their families and/or care givers that are directed toward preventing or minimizing the secondary complications associated with these injuries.
- C. Develop training materials to assist persons with disabilities and their caregivers to safely and efficiently evacuate various

buildings, (e.g., multi-storied structures) in emergencies.

### **Other Research Topic(s) Within Mission of Center**

For programmatic information, contact:

Mr. Ted Jones  
Centers for Disease Control and Prevention  
National Center for Injury Prevention and Control  
Office of Research Grants  
Mail Stop K-58  
4770 Buford Highway, N.E.  
Atlanta, Georgia 30341-3724  
(770) 488-4824; Fax: (770) 488-1662  
Email: [tmj1@cdc.gov](mailto:tmj1@cdc.gov)

For administrative and business information, contact:

Joanne Wojcik  
Centers for Disease Control and Prevention  
Procurement and Grants Office  
Mail Stop E13  
2920 Brandywine Road  
Atlanta, Georgia 30341  
(770) 488-2717; Fax: (770) 488-2777  
Email: [jcw6@cdc.gov](mailto:jcw6@cdc.gov)

### **NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)**

The National center for Chronic Disease Prevention and Health Promotion supports a national program to prevent premature death and disability from chronic disease and to promote healthy personal behaviors.

#### **Arthritis and Other Rheumatic Conditions**

The Arthritis Program in the Division of Adult and Community Health is working to implement the National Arthritis Action Plan-a Public Health Strategy to decrease the burden of arthritis in the United States. Arthritis is the leading cause of chronic pain and disability in the United States. Opportunities exist to reduce the burden of arthritis and its impact by increasing knowledge of arthritis, self management of arthritis, and the importance of physical activity and weight control among both people with arthritis and health care providers.

A. *Self Management Programs and Materials.* There is interest in the development, application and evaluation of innovative interventions to increase self management, including weight control and physical activity, among persons with arthritis. Self management (weight control and exercise) programs have been shown to have beneficial effects for people with arthritis. Although effective strategies for self management exist, few have been adequately implemented. The focus of proposed projects should reflect target populations at high risk of arthritis.

1. Design, develop, and evaluate a CD-ROM or Web-based arthritis self management programs for different population groups that may include low income, minority, elderly, rural, or non-English-speaking audiences.
2. Design, develop, and evaluate education materials (e.g., videos, cassettes, workbooks, etc.) addressing self management for different population groups that may include low income, minority, elderly, rural, or non-English-speaking audiences.
3. Design, develop and evaluate weight control (weight loss) programs and/or materials that are safe and effective for people with arthritis.

B. *Exercise equipment, instructional materials and assistive devices.* There is interest in the development, application and evaluation of exercise equipment appropriate for people with arthritis and other rheumatic conditions. Persons with arthritis need to do both aerobic and resistive physical activity. There is limited amount of exercise equipment that is safe and easy to operate by persons with arthritis who are unable to use existing exercise equipment. Persons with arthritis can also benefit from devices that prevent or minimize functional limitations, and packaged instructions on how to exercise safely with their specific type of arthritis or degree of limitation.

1. Design, develop and evaluate low-impact exercise equipment designed to be safe and easy to operate by people with arthritis and other rheumatic conditions who are unable to use existing exercise equipment.

2. Design, develop and evaluate resistive exercise equipment designed to be safe and easy to operate by people with arthritis and other rheumatic conditions who are unable to use existing exercise equipment.
  3. Develop adaptive equipment, assistive devices, and/or instructional materials directed toward preventing or minimizing functional limitations or preserving independence among persons with arthritis and other rheumatic conditions.
  4. Develop and evaluate instructional materials (i.e. videotapes) on exercise or physical activity that are tailored to different types of arthritis or different levels of disease activity or functional limitations.
- C. *Physician and Other Health care Provider Education/Training.* Methods are needed to increase awareness of self management and develop programs to build self management education and physical activity recommendations into routine care for people with arthritis and other rheumatic conditions.
1. Design, develop and evaluate materials to educate or train physicians and/or other health care professionals on the importance of self management and how to foster increased self management among their patients.
  2. Design, develop and evaluate materials to educate or train physicians and/or other health care professionals on the importance of physical activity and how to foster increased appropriate physical activity among their patients.

For programmatic information, contact:

Joe Sniezek, M.D., M.P.H.  
 National Center for Chronic Disease Prevention  
 and Health Promotion  
 Mail Stop K-45  
 3005 Chamblee-Tucker Road, Chamblee  
 Atlanta, GA 30341  
 (770) 488-5596; Fax: 770-488-5964  
 Email: [jes6@cdc.gov](mailto:jes6@cdc.gov)

For administrative and business information,  
 contact:

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 Centers for Disease Control and Prevention  
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 2920 Brandywine Road  
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## OFFICE ON SMOKING AND HEALTH

The mission of the Office on Smoking and Health is to lead and coordinate strategic efforts aimed at prevention of tobacco among youth, promoting smoking cessation among youth and adults, and protecting nonsmokers from environmental tobacco smoke. Following recent changes in cigarette warning labels in Canada, there is interest in promoting stronger and larger warning labels in the United States as part of a comprehensive program to reduce initiation and promote cessation of smoking.

Warning labels were first mandated for cigarette packs in 1964, with the expansion to rotating messages in 1984. Research suggests however that warnings as they currently exist may not be noticed, and that the messages may be worn out. Canada has had black and white warnings occupying 25% of the front of packs since 1994 and is slated to expand warnings to 50% of the packs in January 2001. In addition to increased size, the new warnings will include color graphics. Research in Canada has demonstrated that persons report that messages that are larger, with strong emotional appeal, and with graphics and pictures are more likely to encourage them to think about stopping (or not starting) smoking. In addition, increasing the size of the message does not have a significant impact on the ability to recognize a "regular brand".

Very limited data on reactions of U.S. citizens to warning labels of different sizes and configurations are available at this time. Such information will be important in providing support for policy change in the United States.

1. Identify consumer response to health warning messages, as it pertains to size, configuration and impact on the decision-making process to smoke or not. The study sample will need to include adult smokers, and teens who are smokers and nonsmokers.

2. Conduct focus groups in US/Canada border areas to obtain information on reactions of U.S. citizens to new Canadian warning labels. Focus groups will include adults and teens, both smokers and nonsmokers.

For programmatic information, contact:

Pascale Wortley, MD, MPH  
1600 Clifton Rd, MS K-50  
Office on Smoking and Health, NCCDPHP CDC  
(770) 488-5707  
E-mail: [pmw1@cdc.gov](mailto:pmw1@cdc.gov)

For administrative and business information, contact:

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## **NATIONAL IMMUNIZATION PROGRAM (NIP)**

NIP will accept SBIR grant applications on the August 1 and December 1, 2001 receipt dates ONLY. Applications for SBIR grants from the National Immunization Program should be submitted to the Bethesda, Maryland address indicated in the application materials, but the application form should be marked prominently: "Please forward promptly to CDC, Atlanta, for technical review by that agency."

The NIP plans, coordinates, directs, and participates in efforts to prevent and reduce illness and premature death through immunization against disease. Activities include: (1) conducting epidemiology, national surveillance, research and technical consultation on designated diseases for which effective immunizing agents are available and on the safety of vaccines; (2) assessing immunization levels at national, state, and local levels; (3) guiding the development of recommendations, guidelines, technologies, and policies for effective, safe, efficient, and economical use of existing vaccines, and for the development and incorporation of new and improved vaccines and associated technologies into disease control programs; (4) providing technical, epidemiologic, scientific, statistical, financial, programmatic, and administrative assistance to

State and local health departments in support of their immunization programs to prevent diseases recommended for vaccination; (5) implementing national outreach, mobilization, and public information activities to increase understanding about benefits and risks of vaccines, to promote the demand for them, and to improve immunization practices among health care providers; (6) designing, developing, and implementing information systems to ensure that all persons are properly immunized with the recommended vaccines; (7) collaborating with the World Health Organization (WHO) and its regional offices and with other CDC Centers/Institutes/Offices (CIOs); in worldwide eradication efforts for polio, and in planning for eradication of other diseases.

## **Other Research Topic(s) Within the Mission of the Program**

For technical information about the needs of the National Immunization Program, contact:

Bruce G. Weniger, MD, M.P.H.  
Assistant Chief for Vaccine Development  
Vaccine Safety and Development Branch  
National Immunization Program (E-61)  
Centers for Disease Control and Prevention  
1600 Clifton Road (E-61)  
Atlanta, GA 30333  
(404) 639-8779; Fax: (404) 639-8834  
Email: [bgw2@cdc.gov](mailto:bgw2@cdc.gov)

For administrative and business management questions concerning SBIR, contact:

Ms. Joanne Wojcik  
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## **NATIONAL CENTER FOR HIV, STD, AND TB PREVENTION (NCHSTP)**

NOTICE: Effective February 16, 2001  
NCHSTP will not accept SBIR applications in response to the PHS 2001-2 Omnibus Solicitation for SBIR/STTR Grant Applications. These topics have been withdrawn. For additional information, contact Ms. Nina Waters, SBIR Administrator, CDC ([jvw0@cdc.gov](mailto:jvw0@cdc.gov)) or 770-488-2805.

## **NATIONAL CENTER FOR ENVIRONMENTAL HEALTH (NCEH)**

**NCEH will accept SBIR applications ONLY on the August 1 and December 1, 2001 receipt dates.**

The National Center for Environmental Health works to provide national leadership, through science and service, that promotes health and quality of life by preventing or controlling those diseases, birth defects, disabilities, or deaths that result from interactions between people and their environment. NCEH directs programs to prevent the adverse health effects of exposure to toxic substances and to combat the societal and environmental factors that increase the likelihood of exposure and disease. NCEH main activities:

- A. National leadership in prevention programs, global health, and the use of human genetic knowledge, tests, and services
- B. Public health surveillance
- C. Applied research: epidemiologic studies; laboratory analyses; statistical analyses; behavioral interventions; operations and systems research
- D. Communication and education
- E. Standards, guidelines, and recommendations
- F. Training and technical assistance of officials of state and local health agencies in preventing and responding to public health challenges

Research topics include, but are not limited to, those identified below.

### **Environmental Hazards and Health Effects**

- A. Noise-Induced Hearing Loss in Children and Young Adults
  - 1. Identification and development of databases for the analysis of noise-induced hearing loss in children and young adults.
  - 2. Development of a surveillance database for noise-induced hearing loss in children and young adults.
  - 3. Development of prevention material for noise-induced hearing loss, including references to the noise produced by common non-occupational exposures.

### **B. Household Exposures to Hazardous Substances**

- 1. Development of a survey instrument and conduct of a survey for consumer products used in homes that contain hazardous substances.
- 2. Development of a database to link consumer products, hazardous substances, and toxicologic data.
- 3. Development of educational materials related to hazardous materials in consumer products found in the home, risks associated with these materials, and prevention strategies.

### **C. Nutritional Supplements. Development of databases for identifying trends in the type, purchase, and/or use of nutritional supplements.**

### **D. Prevention of Heat-Related Deaths Among the Elderly**

- 1. Develop a practical, inexpensive device to alert elderly persons to potential life-threatening temperature extremes in their dwellings, with information on preventive actions to be taken. (For example, a thermometer-like device with easy to read instructions and information on what action to take when a dangerous indoor temperature is reached.)
- 2. Test the utility of a practical and inexpensive device by distributing them to a sample of elderly people and measuring its acceptability and use.
- 3. Developing companion educational materials for radio and TV stations during heat waves.

### **Emergency and Environmental Health Services**

- A. Geographic Information System (GIS) Based Population Estimation and Sampling Software for Natural Disasters and Complex (Refugee) Emergencies
  - 1. Develop a software "add-on" compatible with major GIS packages, including ArcView and ArcInfo, which will simplify and streamline a GIS based population estimation method developed by CDC, for use in natural disasters and international complex

- emergencies. This software will also be able to simplify and guide area-based cluster sampling for public health surveillance.
2. Field test the utility and accuracy of the software by comparing results from other sampling and estimation methods. Outcome indicators should include complexity of use, time, and human resources needed to estimate a population and guide an area based cluster sample.
  3. Develop an operations manual to use the software in conjunction with major GIS packages and common data sources.
- B. Consolidation of Guidelines and Recommendations Regarding Health and Public Health in Humanitarian Emergencies
1. Produce a computer program containing all important guidelines and recommendations pertaining to health and public health in humanitarian emergencies. This may involve obtaining copyright permission to reproduce this material onto a compact electronic data storage medium, such as CD-ROM.
  2. Create software to allow dynamic searches of all materials, manipulation of text, and printing text and graphics.
  3. Test the acceptability of this new reference tool among members of the field staff of non-governmental organizations, donor governments, and United Nations agencies.
- C. Rapid Extraction Device for Chemical Mass Casualties
1. Develop a simple device for the rapid extraction from the contaminated area (hot zone) of non-ambulatory mass casualties resulting from a chemical weapon release. This device will facilitate the rapid removal of victims from the contaminated area to an area more proximate to the decontamination and treatment zones. It will be attached by rope to winches or other similar mechanisms to pull victims to the decontaminated area. By reducing the time of extraction, victims will receive treatment and decontamination

sooner, improving the probability of survival.

2. The device should be inexpensive (EMS units will need multiple devices), easily applied (workers will be wearing cumbersome protective gear), must be free of sharp edges (device should not violate workers' protective suits), and should provide reasonable protection of the victim's head and upper body (they will potentially be dragged over rough terrain).
3. Other requirements include the ability to be used multiple times during the same event, able to be decontaminated after an event, require minimal storage space, and be lightweight. Training in the use of the device should be minimal. Field testing of the device will be necessary to evaluate effectiveness and durability.

## Environmental Health Laboratory Sciences

- A. Coronary Heart Disease. The development of a laboratory technology to standardize and improve the quality and reliability of laboratory tests for cholesterol and other metabolically related lipids and lipoproteins that are known risk factors associated with coronary heart disease is an area in which the SBIR program may be able to contribute to the improvement of diagnostic techniques. Specifically, development and characterization of improved serum reference materials that can be used by NCEH to standardize laboratories that conduct epidemiological and lipid research and clinical trials into the causes and prevention of coronary heart disease.
- B. Cystic Fibrosis and Medium Chain Acyl Dehydrogenase Deficiency. The development of DNA-based materials containing the pertinent mutations for the screening of Cystic Fibrosis (CF) and Medium Chain Acyl Dehydrogenase Deficiency (MCAD) from newborn dried blood spot specimens. The materials should be in the form of blood dried into an FDA-approved filter paper blood collection device. The materials should provide the appropriate DNA sequences that will respond to mutation analysis methods such as DNA amplification by PCR, restriction fragment length polymorphism analysis,

and nucleotide sequencing. This technology will help to standardize and improve the quality and reliability of laboratory tests that are used to screen for CF and MCAD at birth. Currently, there is no commercial source available for the DNA-based materials for these disorders.

- C. Tests for Type 1 Diabetes Associated Autoantibodies. There is a need for development of rapid, reliable, inexpensive screening tests for autoantibodies associated with Type 1 Diabetes. The availability of such tests, which could be used in physician's offices, health clinics, and other diabetes screening settings, would greatly enhance the early detection and intervention of Type 1 diabetes. Currently available methods for Type 1 Diabetes autoantibodies are time consuming and expensive, and are typically based upon radioimmuno assays. Interest is in developing assays which are simple to perform in low-tech settings and would include (but not be limited to) the following: 1) insulin autoantibody (IAA), 2) glutamic acid decarboxylase (GAD), and 3) Islet cell antibodies including cytoplasmic islet cell antibody [ICA] 512.
- D. Enhancement of Blood Glucose Meters to Improve Management of Diabetes. Individuals with diabetes currently use blood glucose meters to monitor short-term therapy effectiveness. However, a blood glucose measurement is simply the endpoint of a complex interplay of diet, medication, and physical activity. In order for the health care provider and the individual to make the best decisions regarding diabetes management, it is important to record all relevant data, particularly dietary intake and medication history data, affecting the fluctuation of blood glucose.
- This project is for development of a hand-held device to facilitate optimal diabetes management. Improvements of the handheld device over current blood glucose meters would include the capabilities to convert food intake data into ADA diabetic exchanges and relevant therapeutic information entered by the patient such as medication and physical activity history. The device would promote better management of diabetes by facilitating compliance with diet therapy, allowing the

individual to quickly record relevant factors affecting diabetes management, and the inclusion of measurement of blood glucose levels.

- E. Rapid Field Tests for Vitamin A Status. There is a need for the development of rapid, rugged field portable, and economical techniques for determining vitamin A status in finger stick or ear-lobe blood samples collected by microcapillary-techniques or on filter paper. Methods may be based on fluorescence, optical density, or any other technique that reliably estimates vitamin A status in humans, but it should correlate to widely accepted "reference" methods such as high performance liquid chromatography (HPLC). Such methods would be highly valuable in global efforts to eliminate vitamin A deficiency, a high priority for WHO, UNICEF, USAID, and many other international agencies. Vitamin A deficiency is a devastating problem especially in developing countries where it contributes significantly to childhood morbidity and mortality, and is a leading cause of blindness in many parts of the world.
- F. Rapid Field Tests for Iodine Levels in Urine and Salt. Iodine deficiency is a global problem affecting millions of people, leading to reduced population IQ, cretinism, goiter, and contributing to thyroid cancer. To facilitate efforts to eliminate this problem, rapid, simple, and inexpensive tests are needed that can determine the concentration of iodine in urine for population screening work, and that can determine the concentration of iodine in salt samples for quality control purposes in iodized salt production. While field tests for iodized salt have been developed in recent years, they have proven to be inaccurate and unreliable. Tests for urinary iodine typically have required complicated laboratory procedures. Simple, reliable measures for field use would be a great help.
- G. Rapid Field Tests or Continuous Monitors for Arsenic in Drinking Water. Drinking water with toxic levels of naturally occurring arsenic obtained from shallow wells is a serious problem in many parts of the world. Recently, this problem has become especially acute in rural areas of the

underdeveloped world because of efforts to improve drinking water sources that unfortunately did not fully consider natural sources of arsenic. The solution requires deep wells, or water treatment at the point of use. However, because of uncertainty about the level of arsenic in water from these improved sources, and because of the need to give attention to the most heavily contaminated existing shallow wells first, there is a need to develop rapid, reliable, and cost effective tests or monitors for water arsenic.

H. *Rapid Field Tests for Iron Deficiency, Iron Deficiency Anemia, and Hemochromatosis.*

Iron deficiency and iron deficiency anemia are serious problems throughout the developing world and in many high-risk groups in developed countries, including the United States. These problems negatively impact societies by reducing work capacity, impairing mental development and learning, and increasing morbidity and mortality, especially women of child bearing age and young children. Conversely, persons with elevated iron stores (a condition known as hemochromatosis) are at increased risk of serious health problems including cardiovascular disease, diabetes, and severe liver problems. There is a need to develop simple, reliable, easy to operate, and cost effective methods for screening for these conditions in populations and for managing individuals receiving intervention treatments. Techniques or devices which are non-invasive or minimally invasive would be most desirable.

I. *Improved Tests for Zinc Status and Zinc Body Stores in Humans.*

The essential element zinc has been shown to be extremely important in human health. Recently it has been especially important as a co-factor in efforts to combat iron deficiency and vitamin A deficiency in the developing world. There is a need to develop simple, reliable, easy to operate, and cost effective methods for screening for zinc deficiency in populations and for managing individuals receiving intervention treatments. There is also a need for improved approaches to assessing zinc body stores.

J. *Environmental Health/Anti-Chemical Terrorism.* There is a need to develop

rapid, reliable, field rugged methods for detection and quantitative estimation of human exposure to environmental contaminants and toxic chemical-based weapons of mass destruction or terrorism. Such methods must be able to sense the presence or absence of such substances quickly and reliably, and provide some estimation of concentration in human urine, saliva, breath, blood, or transpired through the skin.

- K. *Improving Assessment of Children's Exposure to Toxic Substances.* Children tend to be more susceptible to toxic substances than adults because of a variety of differences related to physical and functional characteristics. It is imperative that exposure of children to toxic substances be minimized or eliminated since exposures could result in subtle effects upon children's growth, maturation, and health. Children are generally at greater risk than adults for exposure to environmental pollutants from inhalation because they have a higher respiratory rate; from dermal exposure because they have more exposed surface area; and from ingestion because they have a tendency to play in and eat dirt.

In order to address children's exposures, the following rapid response technology is needed:

1. Development of an "environmental sensor" that would detect concentration levels of volatile organic compounds (VOCs) and particulates at threshold levels that would be harmful to small children.
2. Development of a "soil tester" that would determine the concentration level of various trace metals and other environmental pollutants that might concentrate in soil, where children are likely to play.

**Other Research Topic(s) Within Mission of Center**

For additional information on research topics, contact:

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## **FOOD AND DRUG ADMINISTRATION (FDA)**

FDA will now accept SBIR grant applications on the same schedule as NIH—April 1, August 1, and December 1, 2001.

The mission of the Food and Drug Administration (FDA) is to protect the public health of the Nation as it may be impaired by foods, drugs, biological products, cosmetics, medical devices, ionizing and nonionizing radiation-emitting products and substances, poisons, pesticides, and food additives. FDA's regulatory functions are geared to insure that foods are safe, pure, and wholesome; drugs, medical devices, and biological products are safe and effective; cosmetics are harmless; all of the above are honestly and informatively packaged; and that exposure to potentially injurious radiation is minimized.

For additional information about areas of interest to the FDA, please visit our home page at <http://www.fda.gov>.

## **CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)**

CBER is responsible for ensuring the safety, efficacy, potency and purity of biological and related products intended for use in the treatment, prevention or cure of diseases in humans as well as the safety of the nation's supply of blood and blood products. The primary responsibility of CBER is to review the quality, safety and efficacy of vaccines, blood products, certain diagnostic products and other

biological and biotechnology-derived human products.

CBER's activities include: evaluating the quality, safety and effectiveness of biological products before marketing, and monitoring the pre-clinical and clinical testing of new biological products; licensing biological products and manufacturing establishments, including plasmapheresis centers, blood banks, vaccine and biotechnology manufacturers; AIDS program and policy activities, including research on AIDS therapeutic products, diagnostic tests and vaccines; research to establish product standards, develop improved testing methods and assess the safety of biological products; compliance, lot release program and post market surveillance; meeting PDUFA goals, new research programs, and new regulatory initiatives (managed review process for all products).

## **CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)**

CDER develops FDA policy with regard to the safety, effectiveness, and labeling of all drugs for human use; evaluates new drug applications and investigational new drug applications; develops standards for the safety and effectiveness of all over-the-counter drugs; monitors the quality of marketed drugs through product testing (bioavailability/bioequivalence testing), post marketing surveillance, and compliance programs; develops guidelines on good manufacturing practices; conducts research and develops scientific standards on composition, quality, safety, and efficacy of human drugs.

Drug regulatory research as conducted in CDER is directed at the discovery of new knowledge relevant to drug development, postmarketing drug experience (patterns of drug use and safety), and drug regulation to enhance FDA regulatory decisions. These drug regulatory decisions impact on the development of regulations, guidelines and guidance for the regulated industry and provide clarity and consistency in application of CDER regulatory requirements. These drug regulatory decisions also impact public health by ensuring that marketing drugs are safe and efficacious and that their risk: benefit profile remains acceptable during the market life of a drug. Specific areas of research conducted by the Center include:

Pharmacology/toxicology, microbiology/virology, clinical pharmacology, pediatric issues in drug therapy, postmarketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., datamining techniques), epidemiologic studies of therapeutics using population-based data, regulatory compliance, product quality, and active surveillance methods.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Develop a system for gathering real-time data on physician prescribing behavior, understanding and compliance with drug product labeling and frequency of off-label prescribing.
- B. Develop methods for timely active surveillance of newly approved drug products in large populations to identify both expected and unexpected outcomes.
- C. Develop methods for actively collecting information on all cases of classically drug-associated events (e.g., acute liver failure, blood dyscrasias, severe desquamating skin disorders) to augment the FDA's current passive surveillance system.

#### **CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN)**

CFSAN conducts research and develops standards on the composition, quality, nutrition, and safety of foods, food additives, colors, and cosmetics; conducts research designed to improve the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics; coordinates and evaluates FDA's surveillance and compliance programs relating to foods, color, and cosmetics; reviews industry petitions and develops regulations for food standards to permit the safe use of color additives and food additives; collects and interprets data on nutrition, food additives, and environmental factors affecting the total chemical result posed by food additives; and maintains a nutritional data bank.

#### **CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)**

CDRH develops FDA policy and solves problems related to public health and safety of medical devices and radiation-emitting electronic products. It evaluates applications for premarket approval of medical devices, approves products development protocols and exemption requests for investigational devices. It classifies devices into regulatory categories, develops safety and effectiveness standards and good manufacturing practices regulations, operates postmarket surveillance and compliance programs, and provides technical, non-financial assistance to small manufacturers. The Center also conducts programs to reduce human exposure to hazardous ionizing and nonionizing radiation, through an electronic product radiation control program and other programs designed to control and to limit radiation exposure. The Center develops and conducts research and testing programs in the areas of physical, life, and engineering sciences related to the human health effects of radiation and medical device technologies, provides expertise and analyses for health-risk assessments, and also develops new or improved measurement methods, techniques, instruments and analytical procedures for evaluating product performance and reliability. The overall research program may be categorized into four areas, as follows:

1. Characterization of the constituents or components of products.
2. Measurement of product performance.
3. Bioeffects that derive from human exposure to radiation or medical devices.
4. Radiation metrology in support of Agency regulation of radiation-emitting products.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Develop an optical non-destructive method for rapid microtopographic evaluation and measurement of wear of articulating surfaces of implant prostheses.
- B. Develop a system, including CDROM database of human chemical physiological, electrical and mechanical service environment test parameters, for use to design test protocols for implant device

performance and for accelerated reliability testing.

- C. Develop a system, including database and radiation dosimetry badges, for monitoring and registering radiation exposure (dose) of health care providers during interventional radiologic procedures (e.g., angioplasty, percutaneous renal stain removal).
- D. Perform human factors analysis of design and operation of one or more medical devices such as infusion pumps, defibrillators or endoscopes.

### **CENTER FOR VETERINARY MEDICINE (CVM)**

CVM is a public health organization that enables the marketing of effective drugs, food additives, feed ingredients, and animal devices that are safe to animals, humans, and the environment. The Center, in partnership with Federal and state agencies and other customers, ensures animal health and the safety of food derived from animals. The Center makes timely, quality decisions and takes regulatory actions to ensure that these products provide for quality health care of animals, minimize the transmission of zoonotic diseases, and increase the efficiency of production of animal-derived food and fiber. Regulatory decisions are supported by research, the monitoring of product safety, and efficacy, and the continual improvement of processes.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Development of analytical methods and animal models for animal drug residues in edible tissues and feeds.
- B. Development of in vitro and in vivo models for evaluating the safety and efficacy of animal drugs.

### **OFFICE OF ORPHAN PRODUCTS DEVELOPMENT**

The Office of Orphan Products Development was established to identify and facilitate the development of orphan products. Orphan products are drugs, biologics, medical devices and foods for medical purposes, which are indicated for a rare disease or condition (i.e., one affecting fewer than 200,000 people in the United States). These products may be useful

in a rare disease/disorder but lack commercial sponsorship because they are not considered commercially attractive for marketing. A subcategory of orphan products are those marketed products in which there is evidence suggesting usefulness in a rare disease/disorder but which are not labeled for that disease/disorder because substantial evidence of safety and effectiveness for that use is lacking.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Development of pediatric formulations for already approved products for the specific purpose of submitting data to the FDA to include pediatric labeling to the current label of the approved product.
- B. Development of products for the treatment of rare diseases or disorders including but not limited to neurological, metabolic, genetic, ophthalmologic, hematologic, and dermatological diseases or disorders for the specific purpose of obtaining marketing licensure.
- C. Development of products for use in diagnosis of rare diseases for which the diagnostic tool would be used in fewer than 200,000 persons annually in the United States.
- D. Development of vaccines for the prevention of rare diseases to be used in fewer than 200,000 persons annually in the United States.

### **Other Research Topic(s) Within Mission of FDA**

For additional information on research topics and administrative and business information, contact:

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